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ACUTE OSTEOMYELITIS OF THE VERTEBRAE

HERBERT M. KLEIN, M.D.

NEW YORK

Acute osteomyelitis of the vertebrae constitutes a clinical entity of interest and importance to both the internist and the surgeon. The disease consists of an acute suppurative spondylitis generally consequent on metastatic infection of the vertebrae at the time of a previous bacteremia, occasionally the result of the involvement of the vertebrae by a local inflammation that has spread by direct extension. The malady is serious, is often not recognized promptly and is attended with a considerable mortality. The American literature has paid this subject scant attention. The following sixteen cases, proved by operation or necropsy, have occurred in the Mount Sinai Hospital chiefly during the past seven years and are presented to serve as a basis for the analysis of the disease and its clinical aspects. The aim of this study is clinical. For statistical and theoretical discussions of the subject, the reader is referred to Volkman,[1] Wilensky[2] and Borchers.[3]

CLINICAL CONSIDERATIONS

In general, the history, mode of onset and generic symptomatology of all the cases had many features in common. However, for clinical purposes, it has been possible to subdivide the series into four groups according to the nature of the presenting clinical condition. The latter was usually a complication, e. g., epidural abscess, and often dominated the clinical scene.

History.—It is most important to elicit the history of a preexisting lesion which may have been the focus for a bacteremia. In contrast to osteomyelitis of the long bones, to which the young are so prone and which is so often cryptogenetic, the presumable portals of entry were established in fifteen of the sixteen cases. These included boils and carbuncles, previous chronic osteomyelitis, pneumonia, cellulitis of the

From the Medical and Surgical Services of the Mount Sinai Hospital.

1. Volkman, J.: Ueber die primäre akute und subakute Osteomyelitis purulenta der Wirbel, Deutsche Ztschr. f. Chir. **132**:445 (Jan.) 1915.

2. Wilensky, A. O.: Osteomyelitis of Vertebrae, Ann. Surg. **89**:561 (April) 1929; 731 (May) 1929.

3. Borchers, G.: Ueber die primäre akute und subakute Osteomyelitis purulenta der Wirbel, Arch. f. klin. Chir. **158**:168 (Feb.) 1930.

arm, phlebitis of the hepatic vein radicles subsequent to cholangeitic abscess of the liver, acute bacterial endocarditis of the aortic and mitral valves, cystitis with purulent prostatitis, mastoiditis with mastoidectomy, lateral sinus thrombosis, purulent bronchitis in cachexia (phlebitis of the smaller radicles of the pulmonary vein?) and a secondarily infected hematoma. Typhoid fever, paronychia, alveolar abscess, pharyngitis and mastitis may also be sources of bacteremia with metastatic osteomyelitis.[1] A history of true rigor may be obtained, and is of great significance even though it may have occurred many months before. Trauma played no appreciable rôle in this series of cases.

Mode of Onset.—As well as could be determined, the shortest time in which objective evidence of a local pathologic process developed was ten days (case 2). In all the other cases, at least two weeks were necessary. Generally, a little local pain or rigidity was complained of; this gradually became more severe until there was complementary evidence of local disease. In no case was there sudden onset with severe local symptoms and signs pointing to the underlying processes. *Pari passu* with the aggravation of the local condition was the intensification of the systemic indications of the infection.

Generic Characteristics.—In contrast to the osteomyelitis of the long bones, only two of these cases occurred in children. The patients were all febrile and apparently suffering from an infection, with the customary manifestations of fever, tachycardia, leukocytosis, albuminuria, etc. These observations show the necessity for careful investigation when the process is not superficial and therefore obvious. None of the cases presented the appearance of rapidly fatal overwhelming infection, with signs only of generalized intoxication without localization, which is occasionally seen in osteomyelitis of the long bones. The difference may be due to the relatively small amount of marrow infected, in contrast to the amount involved in disease of the long bones.

The following local characteristics may be common to osteomyelitis of the spine, no matter where situated:

1. There is pain, especially on motion. The aggravation of the pain on motion may be due to the spasm of the contiguous musculature or to pressure on a diseased intervertebral disk. Pain on jolting is often absent and is less prominent than in tuberculous spondylitis.[1]

2. Local tenderness may or may not be present over the spinous processes. It is less apt to be present when only the bodies of the vertebrae are diseased. In two cases pain was maximal over normal vertebrae. In case 10, clinically, tenderness had been elicited over the spinous processes of the second and third sacral vertebrae; however, at necropsy, the osteomyelitic foci were found in the second and third lumbar vertebrae.

3. Signs of local inflammation generally indicate perforation and are most commonly present when the laminae or processes are affected, but may be present in exclusive involvement of the vertebral bodies.

4. There is a grating sensation on palpation, owing to sequestration of a spinous process.[1]

5. Local deformity with actual gibbus may occur, owing to the collapse of the diseased vertebrae, as in case 13. Generally, there is only transient deformity, due perhaps to muscle spasm which disappears with the subsidence of inflammation.[1]

The cases may be divided into the following groups:

Group I. The most frequent clinical picture presented is that of abscess formation. This may occur anywhere along the spine. Although the pathologic process is everywhere essentially the same, the difference in the location of the site involved causes a variety of clinical pictures. In the order of frequency these are as follows:

A. The abscess generally presents in the back, near the vertebral column. The skin over the suppurating area most often reveals no local etiologic lesion (when the process is metastatic in origin). There may be no signs or symptoms of underlying bony disease. In this series, ten days was the shortest period of time for the formation of an abscess large enough to be recognized. At operation bare bone is felt at the base of the abscess cavity. This establishes the osteomyelitic origin of the abscess.

B. The next most frequent situation for the abscess is the region of the psoas magnus muscle. A tremendous collection of pus may be present here and yet not cause a swelling conspicuous enough to be detected by careful physical examination. Its existence may have to be inferred from the presence of tender enlarged inguinal lymph nodes associated with homolateral psoas spasm. When a tuberculous abscess of the spine gravitates along the psoas muscle down to the inguinal region, caseating inguinal adenopathy occasionally develops in a similar fashion, but the swelling created is cold, indolent and generally not tender. Because of the involvement of lumbar nerve roots by the inflammatory process, there may be abdominal distention, pain and rigidity, so that one may be inclined to infer the existence of an acute surgical inflammation within the peritoneal cavity ("acute abdomen"). The presence of costovertebral tenderness, with a local mass or spasm of the lumbar muscles and purulent urine, may lead to the erroneous diagnosis of perinephritic abscess, secondary to a perforated cortical abscess of the kidney. Since this is frequently a concomitant metastatic lesion, the diagnosis may be established with certainty only at operation.

C. An apparently idiopathic abscess may present in the buttock. At operation bare bone may not be felt at the base of the abscess

cavity. In such a case one must investigate the lumbar and sacral vertebrae for the presence of an osteomyelitic focus. A collection of pus arising from these vertebrae may gravitate down along the tissue planes, pass through the major sciatic foramen and present in the buttock. It may also pass over the crest of the ilium and present in the buttock. It is because of this devious route that bare bone is not encountered at operation. The collection of pus may pass through the minor sciatic foramen and present beside the anus. This may be the explanation for a persistently draining ischiorectal abscess.

D. The mediastinum may also be the seat of abscess formation. The patient may complain of pain in the chest or abdomen, a pleuritic friction rub may be heard, and later there may be present an area of dulness with diminution of breath sounds. Constant dry cough and hiccup may occur. The diagnosis of mediastinal abscess is made by (1) a history of a focus capable of giving rise to a bacteremia, (2) localized tenderness over the spinous processes of the thoracic vertebrae and (3) roentgenographic evidence of widening of the mediastinum, like that produced by mediastinal collections of fluid.

Group II. The second most frequent clinical group is that in which the patients present a variety of complaints referable to the nervous system. There may be paresis or paralysis of a limb, sphincteric disturbances, abnormalities in the reflexes, impairment of sensory perception or tenderness along the peripheral nerves. Because of the presence of an infection elsewhere in the body and findings that simulate those of myelitis or peripheral neuritis, an erroneous diagnosis of "toxic myelitis" or "toxic neuritis" is often made. The signs and symptoms are generally due to involvement of the nerve roots by the inflammatory exudate or to compression of the spinal cord, which is consequent on pachymeningitis, epidural abscess, etc., the result of perforation of the osteomyelitic focus. The latter must be suspected when a patient with a history of an inflammatory focus capable of giving rise to a bacteremia shows signs and symptoms referable to disease of the spinal cord. Of great diagnostic value are tenderness over the spinous processes, signs of a level lesion, evidences of spinal subarachnoid block and pleocytosis in the cerebrospinal fluid. This group of related conditions in a patient suffering from an infection is most suggestive of perforation of an osteomyelitis of the vertebrae.

Group III. In this group may be classed those patients who present only pain in the back and fever. No other findings may be elicited despite elaborate efforts to determine the cause of the pain. Symptomatic measures fail to give relief. Roentgenographic examination of the painful segments of the spine may yield negative results despite months of suppuration. Diagnosis is most difficult in these cases and may be established only by operation. When the general clinical picture

indicates the existence of infection and there is a history of previous bacteremia, an exploratory operation may have to be performed, especially when the painful area is tender. It may be fatal to postpone operation until one has the confirmatory evidence of a complication (spinal meningitis).

Group IV. The fourth group includes those patients who suffer from widespread suppuration consequent on a bacteremia. There are multiple abscesses throughout the viscera, e. g., in the kidneys, spleen and lungs, and, coincidentally, abscesses in the vertebrae. The clinical picture produced is a summation of the signs and symptoms due to the suppurative spondylitis, as described in the first three groups, and those dependent on the nature and location of the coincident metastatic abscesses elsewhere and the complications subsequent to them.

The cases comprising this group are least in importance from a therapeutic standpoint. Even if the bone focus is susceptible to adequate treatment, death occurs because of the already established, generalized, metastatic abscesses. However, in cases in which the osteomyelitic focus is itself the source of a bacteremia, often persistent, adequate local treatment may eradicate the focus and terminate the bacteremia; the metastatic foci may heal completely, and the patient may then recover.

PATHOGENESIS

There are two ways in which the vertebral infection may occur. Most frequently, there is a localized infection which gives rise to a bacteremia; bacteria localize in the vertebrae and cause an osteomyelitis. This mode of development is well illustrated by case 10, in which a pneumococcus type I was recovered from the pus in the infected mastoid process, from the blood stream on the day after operation and from the pus in the mediastinal abscess produced by the vertebral osteomyelitis. This development can be traced in cases 5, 10, 11 and 14. In rare instances there is a local inflammation which spreads and involves the vertebrae by direct extension (case 6).

BACTERIOLOGY

In the literature the following have been described as causative organisms: Staphylococcus aureus and albus, Streptococcus pyogenes, Bacillus typhosus, Micrococcus tetragenus,[1] B. paratyphosus A[4] and B. perfringens.[5] In addition to these there were found in this series Streptococcus viridans, the pneumococcus, types I, III and IV, and the Friedländer bacillus. In view of the variety of organisms that have

4. Zanboni, G.: Osteomyelite degli archi vertebrali della II-III-IV lombare da paratifo A, Ann. ital. di chir. **5**:499 (May) 1926.

5. Laborde, J. P. A. M.: Étude sur les spondylites staphylococciques de l'adulte, Thèse, Paris, 1926, vol. 39, no. 93.

already been found responsible, it would not be wise to rule out the diagnosis if there should be isolated from a patient suspected of vertebral osteomyelitis an organism (e. g., B. coli) that has hitherto not been described in this condition (see addendum).

In six of the cases, blood cultures were taken, and in each case bacteria were recovered from the blood stream. In four of the cases, the focus causing the bacteremia was distant from the local bone disease, e. g., hepatic vein phlebitis; in one (case 6), it was the local inflammation, and in one other (case 12), it was a phlebitis, complicating a perforation into the soft tissues of the vertebral suppuration. Depending on the nature of the causative focus, the bacteremia was transient (cases 6 and 10) or lasted until the death of the patient (cases 11, 13, 14 and 15).

PATHOLOGY

Anatomically, the cases can be divided into two groups, depending on whether the bodies or the processes of the vertebrae are the sites of the inflammation. In ten cases the bodies were involved; in eight of these there was frank suppuration, often with abscess formation; in one (case 10), the body was merely denuded of periosteum, roughened and tender, and in one other the nature of the corporeal involvement could not be determined. In only three cases was a bony process found to be the seat of the inflammation. In three cases it was not possible to ascertain definitely which portion of the vertebrae was diseased. In the cases in which the process was involved, the inflammation was chiefly superficial, the exposed bone being merely bare and rough. Perforation was earlier when the inflammation occurred in a process, perhaps because of the smaller volume of bone affected.

It is customary to divide vertebral osteomyelitis into cortical, or subperiosteal, and medullary types. To the former belong the cases that present only superficial infection of the bone, which is denuded of periosteum, rough and tender; they occur chiefly in infection of the processes. To the latter belong the cases with frank suppuration and abscess formation; they occur chiefly in infection of the vertebral bodies. If the necrosis is sufficiently extensive, the body may be crushed.

Worthy of mention is a chronic form of the disease described by Radt.[6] In this condition the process may last for many years, with the formation of an ossifying perivertebral granulation tissue which compresses the nerve roots and produces severe, intractable radicular pains.

In cases of bacteremia, it is probable that organisms are carried to many bones besides those which become diseased. Just why certain vertebrae fall a prey to the bacterial invasion is impossible to state. In one case two widely separated vertebrae were infected, while in four

6. Radt, P.: Ueber chronische Osteomyelitis der Wirbelsäule und des Kreuzbeins, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **41**:389 (May) 1929.

cases two annectent vertebrae were diseased. In only two cases can there be implicated a contributory factor, favoring the development of the metastatic process. In one (case 15) there was an old local spondylitis, and in the other (case 16) Hodgkin's infiltrations were present in the vertebral body.

When perforation occurs posteriorly, a superficial abscess forms; it is readily drained, and convalescence is generally uneventful.

Serious complications are usually consequent on perforations that do not come from the processes or laminae and that are not directed posteriorly. Irrespective of the situation of the disease process, the most frequent and most serious complication is that of involvement of the central nervous system. Compression of the spinal cord may be caused by: (*a*) an epidural abscess, secondary to perforation into the epidural space; (*b*) a subdural abscess secondary to epidural infection; secondary to the subdural infection, spinal leptomeningitis may occur and spread to involve the cerebral leptomeninges; (*c*) a pachymeningitis. In a case described by Fraenkel [7] there was a cervical osteomyelitis secondary to infection of a toe; the signs and symptoms of compression of the spinal cord developed; at necropsy the dura mater adjacent to the osteomyelitic focus was found to be thickened and infiltrated with round and plasma cells, among which there were many organisms resembling staphylococci; there was a definite compression of the spinal cord by the thickened dura; there was no epidural or subdural abscess.

Another complication is that of involvement of a major vascular trunk. In case 12, the purulent exudate, surrounding the right common iliac vein, produced a fatal thrombophlebitis. The inflammatory manifestations noted clinically in the right lower extremity were considered the result of retrograde phlebitis, although no substantiation by anatomic examination was undertaken at necropsy. There is a case described by Plenz [8] in which an intercostal vein, secondarily infected by pus from the dorsal vertebrae, was responsible for a bacteremia with metastatic abscesses and a fatal outcome. This thrombophlebitis had caused a swelling of the overlying soft tissues, which were red and tender. This, clinically, was thought to be due to the burrowing of pus from the diseased vertebrae. At operation no pus was found to explain the soft tissue swelling. The thrombophlebitis was neither suspected nor detected and yet was the most important inflammatory process present. A case of fatal erosion of an iliac artery has been reported.[9]

7. Fraenkel, E.: Ueber Spondylitis acuta infectiosa und Rückenmarkserkrankungen, Fortschr. a. d. Geb. d. Röntgenstrahlen **30**:103 (Jan. 15) 1923.

8. Plenz, P. G.: Ueber Osteomyelitis acuta und subacuta der Wirbel, Deutsche med. Wchnschr. **47**:416 (April 14) 1921.

9. Corret, P.; Michon, P., and Reny, F.: Abcès ostéomyélitique vertébral ayant ulcère l'artère iliaque externe chez un ancien blessé de guerre, Rev. méd. de l'est **57**:259 (May 1) 1929.

There are a number of complications recorded which depend on the location of the diseased vertebrae. In the cervical region the following may occur: (1) direct extension of the inflammatory process to the intracranial cavity, generally with fatal cerebral leptomeningitis [5]; (2) involvement of the roots of the phrenic nerve by the inflammatory granulation tissue or pus, with consequent paralysis of the diaphragm; (3) retropharyngeal abscess with respiratory obstruction, and (4) gravitation of the pus into the posterior mediastinum, with possible secondary perforation into a pleural or the pericardial cavity.

In the thoracic region there may occur: (1) perforation into the esophagus and (2) perforation into the mediastinum, with possible secondary perforation into a pleural or the pericardial cavity.

In the lumbar region the following may occur: (1) psoas abscess, the most common complication of lumbar osteomyelitis and already discussed, (2) perforation into the intestine, with consequent purulent diarrhea, and (3) perforation into the urinary tract, with sudden massive pyuria.

Although signs of peritoneal irritation are not infrequent, actual peritonitis is rare. It is most unusual for a psoas abscess to perforate into the peritoneal cavity.

RÔLE OF THE X-RAYS IN DIAGNOSIS

The x-rays were not of great service in demonstrating the presence of osteomyelitis. Only after bone destruction or new bone formation has occurred may one expect roentgenographic change. In eleven of the cases, roentgenograms were taken. In nine of these cases the examination was undertaken before operation or necropsy revealed the underlying pathologic process. In not a single one of these cases did the roentgenologist report evidence of acute osteomyelitis. The plates were either negative for bone disease or revealed nonspecific hypertrophic spondylitis. George and Leonard [10] also noted this tendency to rapid bone formation. The inflammatory processes in these cases varied in duration from at least a week to nine years. In three cases the roentgenograms were positive. In case 1, roentgenograms were taken one month after operation and showed evidence of osteomyelitis. In case 3, x-ray pictures were taken two days after operation and revealed crushing and fusion of three vertebral bodies, the underlying pathologic process being certainly more than two weeks old; the exact duration could not be ascertained. In case 5 roentgenograms were negative the day before operation, but were positive two and a half weeks after operation. Therefore, in a patient with vertebral

10. George, A. W., and Leonard, R. D.: The Vertebrae, Ann. Roentgenol. **8**:70, 1929.

inflammatory disease the roentgenogram may be negative or reveal only evidence of hypertrophic spondylitis, despite the presence of an abscess in the bone, varying in estimated duration from ten days to four months. It is probable that many of the chronic cases (such as case 14 with gibbus formation) would show roentgen changes, but here the diagnosis is no longer in doubt. It may be that with more frequent roentgenographic examinations, the roentgenogram will prove to be of more value (see addendum).

PROGNOSIS

The prognosis is largely dependent on the following factors: A. The presence and nature of an existing complication. Involvement of the spinal cord offers the worst prognosis, and the formation of an abscess presenting in the back and resulting from a posterior perforation, the best prognosis.

B. The localization of the inflammation in the body or a process of a vertebra. In three of the cases presented, death was due indirectly to the local osteomyelitic focus alone, and in each instance the seat of the disease was in the body of the vertebra. In six cases there were concomitant abscesses in various viscera; in five of these cases, the body was the involved portion of the vertebra, while in the sixth the body of one and a process of another vertebra were involved. In three cases the processes were involved and in two others it is probable that the inflammatory process occurred in the processes. In four of these cases, uncomplicated by infection elsewhere, convalescence was uneventful. The fifth patient is in the hospital at present; his progress is satisfactory. In general, therefore, the involvement of the body carries with it a graver prognosis than does involvement of a process of a vertebra.

C. The promptness of the diagnosis and the adequacy of the surgical treatment.

D. The type of bacterium causing the infection. This does not play a considerable rôle; e. g., case 11, due to Streptococcus viridans, was fatal, while in case 10, due to a pneumococcus type I, and case 4, due to Staphylococcus aureus, the patients recovered.

E. The general resistance of the patient. Although it is undoubtedly a factor, it is difficult to evaluate.

TREATMENT

The treatment is surgical. Concerning it I wish to make only the following comment: A. The primary aim is to drain the suppurating area, especially in order to prevent complications due to perforation.

B. The focus in the bone itself must be drained; it is not sufficient to drain the complicating infection, e. g., an epidural abscess. Radical therapy may not be feasible when the patient is acutely ill, but it is nec-

essary for the accomplishment of a complete cure. Patton [11] described a case in point. In a case of thoracic osteomyelitis, there was removed only some necrotic bone, easily encountered, with the drainage of a small amount of pus. However, because of the progression of symptoms and the development of paraplegia, a second and more extensive operation was necessary after an interval of six weeks; on this occasion the diseased spinous processes and laminae and an exudate on the dura were removed, with the resultant disappearance of the paraplegia and a gradual complete cure.

C. The presence of metastatic foci does not contraindicate operation. The osteomyelitis may be the focus of the bacteremia. Cases of bacteremia with metastatic abscesses of the lung are not infrequent, in which, with the removal of the focus of the bacteremia, the abscesses in the lung heal spontaneously.

D. Recovery may occur after operation despite the presence of bacteria and a pleocytosis in the cerebrospinal fluid (case 6). Signs of compression of the spinal cord were present in this case and disappeared after the drainage of a collection of pus exterior to the vertebral column. Acute inflammatory compression of the spinal cord does not necessarily indicate the presence of more than edema of the epidural tissue and does not warrant a nihilistic attitude, even in the presence of evidence indicating an infected cerebrospinal fluid.

The mortality is still considerable. The following estimates are presented:

Makins and Abbott (Ann. Surg. **23**:510 [May] 1896)	71.4 per cent
Volkman (1914)	41.8 per cent
Borchers (1930)	56.3 per cent
Mount Sinai Hospital (1931) (Case 5 excepted)	51 per cent

DIAGNOSIS

From what has been said, one can see how varied the clinical picture may be. The diagnosis must be entertained whenever any patient who has suffered from an infection presents signs and symptoms referable to a vertebral osteomyelitis. A patient who presents a history of a boil and in whom a sudden paraplegia develops must be investigated for epidural abscess. An apparently idiopathic abscess in the back must have its cause determined before meningitis occurs. One cannot dismiss the diagnosis because a bacterium not generally encountered in osteomyelitis has been obtained in culture. The acute nature (warmth, tenderness, redness, etc.) of the local inflammatory process should differentiate it from tuberculous spondylitis (Pott's disease). In the

11. Patton, C. L.: Acute Osteomyelitis of Spine, Illinois M. J. **57**:268 (April) 1930.

literature, cases have been diagnosed as typhoid fever and cerebrospinal meningitis. In none of this series was this impression created. With the increase of bacteriologic knowledge, the presence of these diseases should be established rapidly. The most frequent diagnostic error has been the failure to consider the possibility of existence of vertebral osteomyelitis. A diagnosis of "toxic myelitis" should be made only after every effort has been made to rule out an epidural abscess.

SUMMARY

On the basis of sixteen cases, the subject of acute osteomyelitis of the vertebrae is presented with an analysis of the nature of the disease, its etiology, its pathogenesis, its clinical aspects, the value of roentgenograms in diagnosis, and some of the considerations underlying the prognosis and the therapeutic approach. The cases themselves are presented in detail as follows.

GROUP I. TYPE WITH ABSCESS FORMATION

CASE 1.—J. W., a man aged 31, was admitted to the hospital on May 6, 1925, with the history of a boil on the neck three weeks before admission, and pain over the left sacro-iliac region, first noticed two weeks before admission, spreading one week later to the left hip and thigh. Since the onset, the temperature had ranged between 100 and 103 F.; sweats had occurred every night, but there had been no chills.

Physical examination revealed tenderness and edema to the left of the lower lumbar vertebrae. Pain was spontaneous and increased on movement of the spine.

Course.—On May 10, there was a sense of deep fluctuation to the left of the fourth and fifth lumbar vertebrae. Aspiration yielded thick yellow pus. A diagnosis of osteomyelitis of the vertebrae was then made.

Operation.—On May 10, operation revealed an abscess cavity containing 4 drachms (15.5 Gm.) of thick pus; in the floor of the cavity bare, rough bone was felt, which was interpreted as the left transverse process of the fifth lumbar vertebra. The cortex of this bone was removed.

Drainage was freed and convalescence uneventful.

Observations.—Bone removed at operation showed osteomyelitis.

Roentgen examination on June 9 showed rarefaction of the left upper articular process of the fifth lumbar vertebra, indicating a probable osteomyelitis.

CASE 2.—G. S., a 61 year old man, entered the hospital on Feb. 6, 1919, with a history of dull pain in the right thigh and lower part of the back for five weeks. Walking was difficult because of the pain.

Physical examination revealed a well nourished man, subacutely ill and supine, with the right hip flexed. Marked rigidity was present over the right half of the abdomen with an indefinite resistance in the right lower quadrant. On the right side of the lumbar spine were two masses, which were tender and fluctuant. The skin was reddened over them and there was marked edema of the entire lower part of the back. A Babinski sign was present on the right. The temperature was 102 F., the pulse rate 80 and the respiratory rate 20. The urine was normal.

Operation.—On February 8, an incision was made in the right costovertebral angle; several ounces of pus were obtained. The abscess cavity led down to roughened bone. On March 3, incision and drainage of the same abscess were again performed; rough bone was felt in the base of the abscess. A pocket of pus anterior to the spine was released and the wound curetted.

Course.—The temperature was normal thereafter and healing progressed uneventfully. The patient was readmitted on June 13. He was operated on twice on the second admission. On August 25, bare bone was felt with the curet. The patient was discharged on September 19, with the sinus healed. In 1921 there was a scant spontaneous discharge from the site of the scar, lasting one week; no operative indication was present.

Observations.—Urinalysis on Feb. 9, 1919, revealed no albumin or sugar; microscopic examination gave negative results.

Curettings removed at operation on March 19 showed chronic inflammatory tissue.

Roentgen examination showed: On Feb. 8, 1919, there was no evidence of a pathologic condition in the lumbar or the six lower dorsal vertebrae, except for a slight degree of spondylitis. On March 6, no evidence of pathologic condition in the lumbar vertebrae was noted. On April 2, the lumbar spine showed evidence of a slight spondylitis; however, a drainage tube present at the site of the right transverse process of the second lumbar vertebrae might have concealed a diseased area in the bone. On April 4, 1921, examination of the lumbar spine showed coalescence of the first and second lumbar vertebrae as seen in cases of old arthritis. On April 6, examination of the lumbar spine after the injection of bismuth showed the bismuth starting at the level of the fourth intervertebral space and reaching up as far as the transverse process of the second lumbar vertebra.

Case 3.—R. F., a boy aged 8 years, was admitted to the hospital on Aug. 18, 1925. He had had osteomyelitis of the right forearm and left femur four years before admission. Since then he had always been ailing. Two weeks before his admission, swelling and tenderness developed in the right lumbar region and he had an afternoon temperature of from 101 to 102 F.

Physical examination revealed, in addition to scars of previous operation on the right forearm and left thigh, a fluctuating, painful and tender mass, 2½ inches (6.3 cm.) in diameter, in the right lumbar region. The diagnosis was lumbar abscess secondary either to a renal abscess or to osteomyelitis of the spine.

Operation.—On August 19, incision and drainage of the abscess were performed. Bare bone was felt in the floor of the abscess cavity.

Course.—With adequate drainage, the wound did well and the patient was discharged on September 21, with only a slight discharge from the sinus tract. A follow-up note on Jan. 4, 1928, stated that the patient was well; no note was made concerning the lumbar region.

Laboratory Observations.—A blood count, on Aug. 19, 1925, showed white blood cells, 14,250; polymorphonuclears, 80 per cent.

A culture of pus from the abscess on August 19 revealed Staphylococcus aureus.

A roentgenogram on August 21 demonstrated evidences of a destructive process involving the bodies of the twelfth thoracic and first and second lumbar vertebrae, with crushing and fusion of these bodies.

Case 4.—I. S., a man aged 45, was admitted to the hospital on March 12, 1926, with the following history. Eighteen years before, he had had osteomyelitis of the right femur. Nine years later he was operated on, and a collection of pus was

found at the level of the first and second lumbar vertebrae behind the psoas muscle. No culture of this pus was taken. For three weeks prior to admission he had been suffering from pain in the back, progressive in nature and accompanied occasionally by fever.

Physical examination revealed evidences of mitral stenosis and insufficiency, probably rheumatic, and swelling, tenderness and spasm of the muscles to the left of the scar of the previous operation in the lumbar region. The temperature was 106 F. The diagnosis was exacerbation of an old osteomyelitis with spontaneous perforation along the scar of the previous operation.

Operation.—On March 15, an incision was made over the swollen area and pus obtained. In the base of the cavity pus was seen oozing from the bone. The necrotic bone was chipped away and the cavity drained.

Course.—The wound did well, and with a minimal discharge still present, the patient was discharged to the care of his private physician.

Laboratory Observations.—Culture of pus revealed Staphylococcus aureus.

The necrotic bone removed at operation was reported as showing evidences of acute osteomyelitis.

On March 13, 1926, roentgen examination of the lumbodorsal spine showed only evidences of hypertrophic spondylitis. In the anteroposterior position the fourth lumbar vertebra did not appear to be normal. However, in the lateral position, nothing was seen to support this view.

CASE 5.—L. G., a 51 year old man, was admitted to the hospital on Feb. 11, 1932. For seven months prior to admission he had had a discharging right otitis media. Four months prior to admission, the right preauricular region of the face was swollen for two weeks. Shortly after this the patient began to suffer from pain in the left flank and left costovertebral angle. There was fever with chilly sensations for eleven weeks prior to admission. A blood culture at another hospital three months before had revealed the pneumococcus type III.

Physical examination revealed a chronically ill looking man who could not move about because of pain in the lumbar region of the back. Both ear-drums were intact. A few shotty lymph nodes were palpable in the right anterior cervical region. The right costovertebral angle was tender, bulging and fluctuant. The left costovertebral angle was full and tender. There was shock tenderness over the lumbar spine. The diagnosis of osteomyelitis of the lumbar vertebrae was made.

Operation.—On February 13, the right and left lumbar spaces were incised. On the right side an abscess cavity containing 8 ounces (226 Gm.) of pus and a sequestrum of the right transverse process of an upper lumbar vertebra were found. On the left side an abscess cavity was encountered at the bottom of which a denuded transverse process of an upper lumbar vertebra was found. There was a communication between the abscesses across the anterior aspect of the spine.

Course.—The patient is still in the hospital with the operative wounds draining. His condition is satisfactory. Exploration of the right transverse sinus on March 13 showed complete obliteration of the sinus owing to a healed thrombophlebitis.

Observations.—A blood count on Feb. 12, 1932, showed: hemoglobin, 47 per cent; red blood cells, 2,890,000; white blood cells, 21,000; polymorphonuclears, 76 per cent.

Urinalysis showed: specific gravity, 1.012, acid, a few single white blood cells and no albumin.

A blood culture on Febrary 12, was sterile. A smear of pus obtained at operation, on February 13, showed gram-positive cocci; no tubercle bacilli were seen.

A culture yielded the pneumococcus type III. A culture of the urine on February 13 showed the pneumococcus type III and Staphylococcus albus.

Roentgen examinations were as follows: On February 12, examination of the spine showed no evidence of osteomyelitis. There was moderate hypertrophic spondylitis of the lower dorsal and lumbar bodies. On March 2, reexamination of the lumbosacral spine showed almost complete disappearance of the right transverse process of the second lumbar vertebra, and an exaggeration of the spondylitis, involving the second and third vertebrae. There was marked clouding of the entire right mastoid process.

Comment.—This is considered to be a case of otogenic sepsis, due to the pneumococcus type III, consequent on a latent spontaneously healing thrombophlebitis of the right transverse sinus, with metastatic infection of the lumbar vertebrae.

CASE 6.—R. V., an infant 2 months of age, was admitted to the hospital on Sept. 10, 1923, with the history of a bluish swelling on the back of the neck, present at birth; this became hard and two weeks later discharged pus, which continued to drain up to the time of admission. For six days before admission, fever had been noticed. For five days the infant had not been able to move her left arm.

Physical examination revealed a reddened area of induration on the posterior aspect of the neck. The infant could not move either arm. The upper extremities showed flaccid hypotonia with anesthesia. The right lower extremity was spastic. Aspiration of the swelling yielded a few drops of pus.

Operation.—On September 12, operation revealed a large collection of pus under tension, deep to the erector spini muscles; in the base of the abscess rough bone was exposed, which was thought to be the left transverse process of the fifth or sixth cervical vertebra.

Course.—The wound healed satisfactorily, the motor and sensory disturbances cleared up and the patient was discharged. Convalescence was uneventful except for a period of aggravation of the symptoms of infection with transient bacteremia about September 22.

Laboratory Observations.—A blood count on Sept. 11, 1923, showed: white blood cells, 40,200; polymorphonuclears, 54 per cent.

A blood culture on September 14 was sterile. On September 22, a culture revealed 200 colonies of Staphylococcus aureus per cubic centimeter.

Cultures of the cerebrospinal fluid showed: on September 12, 24 cells and sterile fluid; on September 22, Staphylococcus albus and Streptococcus anhemolyticus; on September 23, 2 cells; on September 28, sterile fluid; on September 29, sterile fluid.

A smear of the pus from the abscess of neck removed at operation on Sept. 12, 1923, was negative; a culture was sterile.

Comment.—The nature of the swelling present on the back of the neck was not definitely ascertainable. There was no evidence to indicate that a meningocele existed. The primary condition was probably a hematoma, possibly resulting from birth trauma, which became secondarily infected.

CASE 7.—R. A., a woman aged 58, was admitted to the hospital on Dec. 12, 1927, with the history of a sudden onset of pain in the right knee radiating up to

the groin, three months before admission. This persisted, was constant and lancinating and was aggravated by motion and damp weather. At the same time, the patient noted a swelling in the right groin, which was very tender and increased in size. The temperature varied from 100 to 104 F. throughout the three months. There was a loss of 30 pounds (13.6 Kg.), in three months. Roentgenograms of the spine taken outside the hospital were said to have been negative. (There was a vague history of osteomyelitis of the right twelfth rib twenty years before.)

Physical examination revealed a cachectic woman with swollen, tender right inguinal lymph nodes; the abdomen relaxed; there was no tenderness and no masses were palpable. The right knee was flexed and there was pain on extension referred to the groin. There was a small well healed scar over the right twelfth rib. The diagnosis made was that of hidden malignant neoplasm with metastases to the right groin.

Course.—On December 17, spasm of the right psoas muscle was noted, so that abscess of that muscle was suspected. The temperature rose; the patient did poorly and died on December 20.

Laboratory Observations.—A blood count showed: white blood cells 8,300; polymorphonuclears, 80 per cent.

The urine contained no albumin, sugar, casts or red or white blood cells.

A roentgenogram of the spine, taken on Dec. 19, 1927, was reported as showing a marked degree of hypertrophic spondylitis between the bodies of the twelfth dorsal, first lumbar and transverse processes of the second, third and fourth lumbar vertebrae on the left side. The left twelfth rib was markedly thickened and irregular, with areas of possible destruction. The eleventh rib also showed similar changes. The appearance of the bones suggested an inflammatory rather than a malignant process.

Autopsy.—Postmortem examination revealed a large retroperitoneal abscess along the course of the right psoas muscle containing 1 liter of greenish pus, compressing and destroying the psoas muscle. The posterior wall of the abscess was formed by dense scar tissue extending upward to the eleventh rib. The bodies of the third and fourth lumbar vertebrae were found to be eroded. The body of the third lumbar vertebra contained a rather old abscess lined by a membrane of granulation tissue near the posterior surface. There were several small abscesses in the fourth lumbar vertebra.

Pus from the psoas abscess contained hemolytic streptococci and B. pyocyaneus on culture; smear showed only gram-positive cocci in chains.

Comment.—This, then, was a case of purulent osteomyelitis of the lumbar vertebrae with the formation of a tremendous retroperitoneal abscess. The primary focus may have been an osteomyelitis of the twelfth rib on the right side, twenty years before. However, the existence of this lesion was not definitely remembered. At autopsy the ribs were not examined.

Case 8.—L. A., a woman aged 44, was admitted to the hospital on Nov. 21, 1928. She had a history of diabetes for ten years. Two years prior to admission, she suffered from a carbuncle of the neck subsequent to which there was a series of abscesses in the right foot and leg, left leg, right clavicular region and left thigh. She entered because of pain in the right hip, knee and leg, with anorexia and vomiting for three weeks.

Physical examination revealed an undernourished, undersized woman with tenderness over the right costovertebral angle and over the spinous process of the twelfth thoracic and first and second lumbar vertebrae. The diagnoses made were abscess of the right psoas muscle and osteomyelitis of the left tibia with subperiosteal abscess.

Operation.—Five ounces (141 Gm.) of pus was evacuated from the abscess of the right psoas muscle; bare bone was not felt. Incision and drainage of the subperiosteal abscess of the left leg were also performed.

Course.—Both wounds discharged large amounts of thick pus. Postoperatively, the patient did poorly. The diabetes was not controlled well, and at one time the patient sank into stupor with ketosis, from which she was resuscitated. On Jan. 27, 1929, pain over the lower cervical spine was noticed. There was edema of the face and hands. A week later the patient began to complain of pain in the neck. There was swelling with some induration over the lower cervical region with a sense of deep fluctuation. There was marked local tenderness with pain on motion. On January 16, incision and drainage of a posterior cervical abscess, apparently extending to the spinous process of the seventh cervical vertebra, were performed. The patient did poorly and died on February 6.

Laboratory Observations.—A culture of pus from the abscess of the psoas muscle on Nov. 27, 1928, revealed Staphylococcus albus. A culture of pus from the subperiosteal abscess of the left leg on November 27 revealed Staphylococcus albus. A culture of pus from the cervical abscess on Jan. 27, 1929 revealed Staphylococcus aureus.

A roentgenogram taken on Nov. 24, 1928, showed bony abscesses in the left tibia. On Jan. 14, 1929, a roentgenogram of the cervical spine showed no abnormality in the bones, although there was an absence of the normal cervical lordosis. Whether this was due to the posture of the patient or to an inflammatory process could not be stated.

Autopsy.—Postmortem examination revealed an abscess cavity, 1 cm. in diameter, in the right transverse process of the third lumbar vertebra. From this region pus extended beneath the muscles along the inner surface of the ilium. It was this area behind the psoas muscle which had been drained by the operation. There was also osteomyelitis of the fifth cervical vertebra and of the left tibia. In addition, there were multiple metastatic abscesses of the right kidney, heart and lungs, with pyopneumothorax.

Comment.—This case was that of a patient with long-standing diabetes on whom a carbuncle developed, with resultant bacteremia and metastatic abscesses situated in the viscera and bones.

Case 9.—D. R., a woman aged 59, was admitted to the hospital on Oct. 7, 1928, with a history of infection of the respiratory tract four weeks before admission, lasting ten days, ending by crisis and diagnosed by her physician as "pneumonia." Three weeks before admission she began to experience a dull ache in the right buttock, accompanied by tenderness on pressure, local heat and swelling. These symptoms progressed in severity up to the time of admission.

Physical examination revealed a circumscribed swelling of the right buttock with questionable fluctuation. No redness over the swelling and no glycosuria were observed. A diagnosis of abscess of the buttock was made.

An operation was performed on October 7. A large abscess cavity containing thick, greenish pus was found extending mesially to the periosteum over the sacrum, which was apparently intact.

Course.—The abscess was draining satisfactorily and the patient was doing well when, on October 24, she had a chill lasting twenty minutes and later complained of abdominal pain and tenderness. The same day, tenderness and distention became marked, and signs of fluid in the abdomen were present. Abdominal puncture was performed and pus obtained. The patient died the next day, October 25.

Laboratory Observations.—A blood count on October 24 showed: white blood cells, 13,600; polymorphonuclears, 83 per cent.

The urine was normal.

A smear of fluid obtained by abdominal puncture showed gram-positive diplococci surrounded by capsules. In a culture of abdominal pus (obtained on October 24) the pneumococcus type IV was grown.

Autopsy.—Postmortem examination revealed small necrotic abscesses in the bony substance of the third and fourth lumbar vertebrae. These communicated by a fistulous tract with the incision in the right buttock. There were also fresh adhesions over the right lower lobe of the lung. There was a generalized purulent peritonitis, consequent on perforation of a secondarily infected echinococcus cyst of the liver. A culture of pus from the vertebral abscess revealed the pneumococcus type IV.

Comment.—This is a case of respiratory infection, probably pneumonia of the right lower lobe (fresh adhesions were found there post mortem), with bacteremia, metastatic infection of the third and fourth lumbar vertebrae and a preexisting echinococcus cyst of the liver. The latter ruptured and produced a fatal peritonitis. Of interest are the following considerations:

1. The condition presented itself as an abscess of the right buttock. The etiology, namely, osteomyelitis of the vertebrae, was not established at operation nor was it suspected clinically.

2. No mention was made of tenderness over the spine in the physical examination.

Case 10.—I. F., a youth, aged 19, was admitted to the hospital on March 11, 1928, with a history of severe pain in the right ear a month before admission. The day after the onset of the pain, myringotomy was performed and a thin purulent discharge escaped from the middle ear. The patient was doing well until three days before admission, when the discharge ceased. Two days later he again had severe pain in the right ear with a thick discharge, thicker and more profuse than previously. One week before admission he had had a chill lasting five minutes.

Physical examination revealed an acutely ill young man, with a temperature of 103.4 F., a thick, purulent discharge from the right middle ear, sagging of the canal wall and impairment of hearing. The diagnosis of acute mastoiditis was made.

Operation.—The patient was operated on on March 11. The mastoid process contained a few scattered small abscesses with little breaking down of the bone.

Course.—On March 12, there was a chill. The patient complained of headache and a bilateral Kernig sign was present. On March 13, the patient began to complain of pain in the right upper quadrant of the abdomen. This was considered pleuritic. On March 16, a pleural friction rub was heard over the right side of the chest anteriorly with diminished breath sounds. Thereafter dulness developed over

the right side of the chest posteriorly. On March 30 an abscess in the right buttock, which had gradually been forming, was incised and drained. On April 19, there was tenderness of the spinous processes of the seventh and eighth dorsal vertebrae. On April 10, pus was aspirated from the right side of the chest posteriorly.

Operation.—On April 10, thoracotomy was performed with resection of the seventh and eighth ribs on the right side. A well encapsulated cavity was found the lateral wall of which was interpreted as the external surface of the parietal mediastinal pleura. The mesal limit was the under surface of the ribs noted, and the anterolateral aspects of the bodies of the seventh and eighth dorsal vertebrae were laid bare. There was a recess leading to the body of the seventh vertebra, but at that point bare bone could not be felt. In contrast to the other, this vertebral body was tender to pressure. The abscess cavity was drained, and the patient recovered completely after an uneventful convalescence.

Laboratory Observations.—On March 11, 1928, pus from the middle ear yielded the pneumococcus type I on culture. A blood culture on March 12 revealed the same organism. Three subsequent blood cultures were sterile. A culture of pus from the abscess in the buttock on March 30 was reported as showing gram-positive diplococci overgrown by Staphylococcus albus. Pus from the mediastinal abscess on April 10 revealed the pneumococcus type I.

On March 19, a roentgenogram of the chest showed a shadow extending anteriorly from the mediastinum, considered to be a partial consolidation of the mesial half of the right lung. On April 3, a roentgenogram of the chest showed this shadow to be more extensive, denser and more sharply demarcated.

Comment.—This is interpreted as a case of acute mastoiditis with transient bacteremia after mastoidectomy, consequent metastatic abscess of the seventh thoracic vertebra, perforation and a resultant mediastinal abscess.

GROUP II. TYPE WITH SYMPTOMS OF DISEASE OF THE NERVOUS SYSTEM

CASE 11.—A. D., a woman, aged 47, had a cholecystectomy performed in October, 1926. At that time the operating surgeon reported the presence of only a single large gallstone. The patient was well until March, 1927, when she began to suffer from severe pain in the right upper quadrant of the abdomen, chills, fever and jaundice. In May, she was operated on at another hospital for the relief of these symptoms. However, a few weeks before her admission on Feb. 29, 1928. she began to suffer from abdominal pain, chills and fever.

Physical examination revealed an acutely and chronically ill woman, with jaundice, a temperature of 103.8 F., two operative scars in the right upper quadrant of the abdomen and some tenderness in the epigastrium. The diagnosis was obstruction of the common bile duct with cholangeitis.

Operation.—On March 3, the patient was operated on; a large mass of exudate was found around the common duct and porta hepatis. The common duct was dissected free and a tube placed in it, resulting in the immediate escape of bile.

Course.—Postoperatively, although there was adequate drainage of bile, the patient continued to have a high septic temperature, fluctuating between 99 and 105 F. On March 22 she began to complain of pains and paresthesias in both legs.

Knee jerks and ankle jerks were absent. There were tenderness of muscles and along the nerve trunks and impaired sensory perception, involving chiefly pain, temperature and deep muscle sensibility in both lower extremities. The diagnosis was toxic neuritis due to the long-standing infection. On March 24, the patient began to suffer from inability to void properly. On March 28, it was noted that she had a subfebrile temperature with occasional attacks of high fever. There was marked paresis of both lower extremities with beginning foot-drop, loss of both knee jerks and ankle jerks, loss of all forms of sensation in the left leg from the midcalf down and in the right leg from the knee down, and tenderness over the second and third sacral vertebrae. On March 31, the diagnosis made was epidural abscess with secondary involvement of the spinal cord at the level of the tenth dorsal vertebra. On April 1, the temperature began to mount again, the patient complained of headache, there was some rigidity of the neck and the general condition was poorer. The Queckenstedt test was performed, with the needle in the third lumbar interspace. The inpression was that no block existed. Cerebrospinal fluid removed showed evidence of meningitis, but there were no clinical indications of cerebral infection. A Queckenstedt test performed on April 3 indicated the probable presence of spinal cord block. On April 4, the mentality was still clear. The next day the patient became irrational, irresponsive and later stuporous; the pulse became rapid and feeble, and death occurred on April 5.

Laboratory Observations.—A blood count on March 12, 1928, showed: white blood cells, 5,000; polymorphonuclears, 48 per cent.

Urinalysis on March 1 revealed bile, urobilin, albumin and white blood cells.

On March 1 a blood culture showed Streptococcus viridans; on March 5, no growth, on March 12, Streptococcus viridans.

On April 1, the cerebrospinal fluid was turbid and contained 10,000 cells per cubic centimeter, with 98 per cent polymorphonuclear leukocytes. Only gram-positive cocci were seen on smear. These failed to grow in cultures.

Autopsy.—Postmortem examination revealed a purulent cholangeitis with multiple abscesses of the liver, one of which had invaded the main right hepatic vein, causing thrombophlebitis at that point. One centimeter from the porta hepatis there was complete stricture of the common bile duct. There were widespread metastatic abscesses in the viscera. The third lumbar vertebra was the seat of a wedge-shaped area of necrosis communicating with the epidural space. There was an epidural abscess extending from the third lumbar to the ninth thoracic vertebra. The body of the second lumbar vertebra presented several softened areas in the bone communicating with the spinal canal by means of a perforation through which a probe could be passed. Exposure of the spinal canal, in so far as it was possible, revealed the presence of a subdural abscess extending from the cauda equina to the highest point of the incision permitted (the limit was not stated; it was probably up to the midthoracic vertebrae). There was also a purulent leptomeningitis. A smear of the pus from the vertebrae revealed gram-negative bacilli (probably a postmortem invader). Cultures were not taken.

Comment.—This case was one of stricture of the common bile duct with resultant cholangeitis and cholangeitic abscesses of the liver, thrombophlebitis of the hepatic vein with resultant bacteremia and multiple metastatic abscesses. Some of these had occurred in the bodies of the second and third lumbar vertebrae, whence there occurred perforation into the epidural, then into the subdural and finally into the

spinal subarachnoid space, causing fatal leptomeningitis. This case was diagnosed in vivo. Of interest are the following considerations:

1. Clinically, tenderness had been elicited over the spinous processes of the second and third sacral vertebrae; however, at postmortem examination the osteomyelitic foci were found to be in the second and third lumbar vertebrae.

2. The first indication of the presence of vertebral disease was that of pressure on the nerve roots.

3. Although examination of the brain was not permitted at necropsy, undoubtedly a cerebral leptomeningitis must have been present. The spread of the infection from the spinal to the cerebral leptomeninges could be followed by parallel changes in the clinical condition of the patient, i. e., at first only signs of spinal cord disease and later the headache, irrationality, and stupor of cerebral disease.

CASE 12.—I. G., a 43 year old man, with a known history of diabetes for six months, entered the hospital because of pyuria, frequency and dysuria, beginning two months before admission. Later there developed urinary retention and dribbling. For two weeks there were numbness and weakness of both lower extremities, progressive up to the time of admission. Eight days before admission a bedsore developed over the sacrum.

Physical examination revealed a weakened, chronically ill looking middle-aged man. There was a large decubitus ulcer over the sacrum and buttocks. Below the level of the seventh dorsal vertebrae there was a loss of all sensation, muscular power and deep reflexes. The patient was considered to be suffering from a transverse myelitis, toxic in nature, due to cystitis.

Course.—The patient did poorly, and died the day after admission.

Laboratory Observations.—The urine contained a large amount of pus.

Autopsy.—There was a purulent cystitis with a prostatic abscess. In addition, there was an epidural abscess extending from the ninth dorsal to the sixth cervical vertebrae with extension into the right thoracic cavity and consequent fibrinopurulent pleurisy. In the muscle there was a walnut-sized abscess just opposite the intervertebral foramen between the spinous and right transverse processes of the ninth dorsal vertebra which had perforated into the epidural space. No evidence of osteomyelitis was found.

Comment.—This is interpreted as a case of purulent prostatitis with a metastatic abscess, situated in the muscle immediately opposite an intervertebral foramen, which perforated into the epidural space. Of interest are the following considerations:

1. The complication, epidural abscess, may so dominate the clinical picture that the primary etiologic condition may be clinically silent. On examination of the patient, it may be impossible to differentiate a case such as this one from one of epidural abscess secondary to osteomyelitis of the vertebra.

2. Osteomyelitis of the vertebra is not the only cause of epidural abscess.

GROUP III. TYPE WITH PAIN IN THE BACK AND FEVER

CASE 13.—C. G., a woman, aged 56, was admitted to the hospital on Sept. 11, 1930, with a history of an infection of a finger of her left hand four months before. This was followed by swelling, tenderness and redness of the entire left arm, chills, a temperature up to 106 F. and general weakness. The diagnosis was erysipelas. The fever subsided after ten days, and there followed slight desquamation of the skin of the arm. For two weeks thereafter the patient was weak. Two weeks later (three months before admission), she began to have a sharp hammering pain beginning in the sacral region, extending to both hips and thighs, occurring daily, worse at night, aggravated by motion and baking, and relieved only by drugs taken on the day before admission. Eight days before admission she was seized with a severe paroxysm of pain in the neck necessitating her going to bed. That night there was delirium. Thereafter there were a high temperature, ranging from 101 to 105 F., profuse sweats and loss of appetite. The day before admission the patient began to suffer from dyspnea and cough, with only slight expectoration.

Physical examination revealed an acutely ill woman, aged 56, who breathed rapidly, with a slight expiratory grunt, coughed occasionally, without the production of sputum, and had flushed cheeks. The temperature was 102 F., the pulse rate 110 and the respiratory rate 26. There was some dulness, with numerous coarse clicking râles over the base of the right lung where the breath sounds were somewhat diminished. There were no signs of fluid or tenderness of the ribs. There was tenderness in the right costovertebral angle. There was some tenderness on percussion over the lumbosacral and sacro-iliac articulations. The diagnosis made was that of bronchopneumonia of the right lower lobe and chronic sacro-iliac arthritis.

Course.—The clinical signs over the right lower lobe persisted unchanged. Because of tenderness over the right costovertebral angle, the diagnosis of metastatic abscess of the right kidney was temporarily entertained. About a week after admission, the patient began to have tenderness in the region of the liver. It was thought that she might have osteomyelitis of the rib and, therefore, two aspirations were made (September 18) at the level of the right fourth rib without encountering pus. A day later the patient began to complain of pain in the legs. There was cutaneous hyperalgesia present but no definite evidence of a spinal cord lesion. There was no appreciable tenderness over any portion of the vertebral column. There was a persistent plateau temperature, averaging about 104 F. On September 19, a diffuse, tender, erythematous pitting induration was seen on the posterior aspect of the right leg. This process spread progressively up to the thigh. On September 20, the patient had a slight chill, which was the first observed since admission. On September 21, exploratory aspiration of the right groin was performed; there was no pus, but some oily droplets were obtained. The patient became jaundiced, sank into stupor and died on September 22.

Laboratory Observations.—A blood count on September 11 showed: white blood cells, 18,700; polymorphonuclear leukocytes, 84 per cent.

Urinalyses on September 11 to 20 showed albumin, one plus, and a few single and very few clumped white blood cells.

Cultures of the urine on September 11, 17 and 20 yielded B. coli. A blood culture on September 11 was sterile; on September 16 a culture yielded 33 colonies of Streptococcus hemolyticus per cubic centimeter; on September 21, 225 colonies of Streptococcus hemolyticus per cubic centimeter.

On September 12, a roentgenogram of the chest showed thickening of the pleura over the right lower lobe with possible calcification. On September 16, a roent-

genogram of the abdomen, taken because of the postulated diagnosis of right perinephritic abscess, revealed only dilated bowel containing much gas.

Autopsy.—Postmortem examination revealed a suppurative spondylitis and perispondylitis involving the bodies of the fifth lumbar and first sacral vertebrae, with softening and purulent destruction of the intervening intervertebral disk. This process had spread anteriorly, causing a suppurative inflammation of prevertebral fatty tissue with suppurative thrombophlebitis of the right common iliac and external iliac veins.

Comment.—This is interpreted as a case of osteomyelitis of the vertebrae consequent on a bacteremia, probably present at the time of the infection of the left arm four months before admission. The suppurating focus perforated anteriorly and produced a purulent thrombophlebitis of the right common iliac vein with consequent overwhelming bacteremia and a fatal outcome. In the light of the postmortem knowledge, the process in the right calf, noted clinically, was considered to be due to retrograde phlebitis of the veins of the right lower extremity, although this was not definitely determined at necropsy. Of interest are the following considerations:

1. Although there was some tenderness over the sacrum and the sacro-iliac joints on admission, this did not increase and was not more marked than that elicited over the rest of the spine.

2. A flat x-ray plate of the abdomen was taken on September 16, because one of the diagnoses under consideration was a right perinephritic abscess. While it is true that this roentgenogram was not taken for the specific purpose of detecting the presence of osteomyelitis in the lumbosacral spine, nevertheless, at the time the roentgenogram was taken, the patient undoubtedly had had the inflammatory process in the vertebrae for about four months; yet on retrospect consideration of the x-ray plate, no evidence of disease in the fifth lumbar or first sacral vertebra (no lateral view) could be seen.

3. There was no clinical index of local inflammatory disease except the complaint of pain.

GROUP IV. TYPE WITH WIDESPREAD SUPPURATION

CASE 14.—D. A., a man, aged 60, was admitted on Oct. 5, 1926, with a history of severe pain in the left side of the abdomen and back, chills, fever and profuse sweats for three days.

Physical examination revealed a well developed man of 60, not looking especially ill; the tongue was coated and the pharynx reddish and dry; dulness and numerous moist râles were noted at the base of the right lung posteriorly and an inconstant sense of resistance in the right upper quadrant of the abdomen; the liver could be percussed three fingerbreadths below the right costal margin. The temperature was 98.2 F., the pulse rate 78 and the respiratory rate 20. The blood pressure was 122 systolic and 80 diastolic. The diagnosis of resolving bronchopneumonia at the base of the right lung was made.

Course.—On October 6 the patient had a chill with a rise in temperature to 104 F. Tenderness and spasticity over the right side of the abdomen and the right lumbar region were noted. A catheterized specimen of urine contained pus and a faint trace of bile. The diagnosis of right pyonephrosis was made. On October 8, a chill occurred. On October 9, cystoscopy with ureteral catheterization showed numerous white blood cells coming from both kidneys, with a few clumps of white blood cells from the right side. On October 11, herpes labialis appeared; a note was made of thick tenacious sputum. On October 13 and 20, a chill occurred. On October 21, the suspicion of a right subphrenic abscess was entertained; the right half of the diaphragm moved less than the left. The liver and subphrenic space were aspirated; no pus was encountered. On November 1, the patient had a severe shaking chill. He complained of pain in the right upper quadrant. The only physical finding elicited in the abdomen was voluntary spasm. Later that day, tenderness and a mass in the right upper quadrant developed, the conjunctivae became icteric and the liver was tender to percussion. A hepatic abscess was suspected. Bile was found in the urine the next day. On November 12 there was no disturbance in motion of the right side of the diaphragm and no tenderness over the liver on jarring. On November 20 the patient complained of pain in the lower part of the back. On November 28 he had severe pain in, and marked tenderness over, the sacrum. A low grade fever persisted. There was a varying leukocytosis.

The patient was discharged at his own request on December 2. He was readmitted on Jan. 26, 1927. He was emaciated and moribund, and kyphosis had developed over the lower part of the spine since his discharge. In the interim he had been fairly well, and had spent most of the time in bed; the only complaint was pain in the back on rising. On the day of admission, he had two severe chills, followed by profuse sweats. The temperature was 104 F., the respiratory rate 30 and the pulse rate not obtainable. The patient did poorly and died a few hours after admission.

Laboratory Observations.—Blood counts showed: on October 6, 1926, white blood cells, 41,800, and polymorphonuclears, 92 per cent; on October 7, white blood cells, 24,400, and polymorphonuclears, 94 per cent; on October 16, white blood cells 10,400, and polymorphonuclears, 76 per cent; on November 11, white blood cells, 29,000, and polymorphonuclears, 88 per cent; on November 29, white blood cells, 20,000, and polymorphonuclears, 86 per cent.

On Oct. 7, 1926, a culture of the blood yielded the Friedländer bacillus, 300 colonies per cubic centimeter in twelve hours. On the patient's readmission on Jan. 26, 1927, a culture showed: 145 colonies of the bacillus per cubic centimeter in twelve hours. On Oct. 8, 1926, a culture of the sputum yielded the Friedländer bacillus. In cultures of the urine on October 12 to 20 the Friedländer bacillus was found three times. The Wassermann reaction of the blood was negative.

From Oct. 6, 1926, to the time of the patient's discharge urinalysis repeatedly showed many white blood cells, often clumped. The reaction to the albumin test was always one plus. On November 2, bile and urobilin were present; on November 3, bile.

On Oct. 6, 1926, a roentgenogram of the chest showed deficient aeration of the base of the right lung perhaps due to a recent pneumonia. The right side of the diaphragm was slightly elevated. On October 12, the lungs showed no abnormality; the right side of the diaphragm was somewhat elevated, but not sufficiently to warrant the diagnosis of a subphrenic abscess. On November 13, the dorsolumbar spine showed a marked degree of hypertrophic spondylitis. On November 20, a roentgenogram of the chest revealed few small infiltrations of a resolving pneumonia at the base of the right lung.

Autopsy.—Postmortem examination revealed an emaciated man with a kyphosis in the region of the first lumbar vertebrae. The lungs were normal except for fibrous pleural adhesions. In the abdomen, between the hepatic flexure of the colon, liver, gallbladder and first portion of the duodenum, there was a loculated abscess containing thick green pus. In the papilla of Vater was a facetted pigment stone, 15 mm. in diameter; the common duct was not inflamed, but was greatly dilated (30 mm. wide when open) and filled with greenish-yellow pus. A few other stones were found in the bile passages. The neck of the gallbladder opened directly into an abscess in the right lobe of the liver adjacent to it, the size of a large apple. This contained greenish pus, and its wall consisted of a shaggy necrotic membrane. Parts of the necrotic walls of the gallbladder were still attached to portions of the wall of the abscess. A direct extension of the hepatic duct entered the abscess cavity. One of the smaller branches of the left division of the portal vein lying in the abscess area had become invaded and contained a purulent thrombus, which extended a considerable distance proximal and distal to its seat of primary involvement by retrograde thrombosis, but the main stem of the portal vein was free.

The kidneys were macroscopically normal; microscopically they showed cloudy swelling, infiltration of the stroma with lymphocyte and leukocyte cells and the formation of many small abscesses.

The prevertebral tissue in the region of the lumbar spine was thickened and suppurated. The first lumbar vertebra was in part destroyed, including the intervertebral disk between the first and second lumbar vertebrae.

A culture of pus from the hepatic abscess and first lumbar vertebra showed Friedländer's bacillus (Bacterium mucosum-capsulatum) in all cultures. Smears showed pus and gram-negative bacilli.

Comment.—In this case one cannot be certain whether the suppurative cholangeitis, due to Bact. mucosum-capsulatum, was primary or whether there first occurred a pneumonia caused by that organism, with bacteremia and metastatic infection of the biliary passages, obstructed by calculi in the common bile duct. The abscess of the liver was probably secondary to cholangeitis. Although no gross thrombophlebitis of the hepatic vein radicles was demonstrated, the hepatic abscess was probably the cause of the bacteremia leading to the renal and vertebral abscesses. However, all the pathologic processes found at necropsy may have been due to a bacteremia at the onset of the disease with a pneumonia due to Bact. mucosum-capsulatum. Of interest are the following considerations:

1. The unusual occurrence of a case of osteomyelitis due to Bact. mucosum-capsulatum (Friedländer's bacillus).

2. The acute development of a gibbus due to suppurative nontuberculous spondylitis.

Case 15.—J. R., a man, aged 30, was admitted to the hospital on Oct. 13, 1930, with the history that ten days before admission a boil developed on the back of the neck, which he squeezed during the subsequent two or three days. This was followed by complete healing of the abscess a few days later. Four days before admission, a mild pain developed in the interscapular region which rapidly became worse. On motion, the patient had sharp pain locally, with radiation down the left

side. On the next day he began to feel feverish. One day later, two days before admission, he had a shaking chill lasting an hour, which was repeated the night before admission. For the three days prior to admission, he had marked anorexia, general malaise, headache, profuse sweating and constipation.

Physical examination revealed an acutely ill man complaining of pain in the midthoracic spine. There was the scar of a well healed abscess on the back of the neck. Flexion of the neck was limited by pain in the midthoracic region, presumably due to spasm of the muscles. There was a short systolic murmur at the apex. No diastolic murmurs were heard. There was some fulness of the prostate with questionable tenderness. There was exquisite tenderness over the spinous process of the fifth thoracic vertebra with some tenderness over the spinous processes of the fourth and sixth thoracic vertebrae. To the right of the fourth thoracic vertebra there was some slight tenderness and fulness of the soft tissue. There was bilateral costovertebral tenderness. The diagnosis was Staphylococcus aureus sepsis with metastasis to the spine (fifth thoracic vertebra).

Course.—On October 14 a Kernig sign developed on the left, the knee jerks were depressed and the upper abdominal reflexes were diminished. Abdominal reflexes were not elicited on October 15. At this time, a prominence of the soft tissue was seen to the left of the spine at the level of the fourth and fifth thoracic vertebrae, construed as indicating deep suppuration.

Operation.—The patient was operated on on the night of October 15. There was no free pus found to correspond to the swelling of the soft tissue. The laminae of the fourth, fifth and seventh thoracic vertebrae were removed; the fifth thoracic seemed definitely sclerosed. An extensive epidural abscess was encountered and drained.

Course.—The patient did not do well, and died on October 19, three days postoperatively.

Laboratory Observations.—A blood count on October 13 showed: white blood cells, 18,000; polymorphonuclears, 78 per cent.

On October 14 the urine showed albumin, one plus, but was otherwise normal.

Cultures of the blood showed: on October 13, 7 colonies of Staphylococcus aureus per cubic centimeter; on October 17, Staphylococcus aureus colonies too numerous to count.

On October 14, a roentgenogram of the spine showed evidences of an old lesion at the level of the fourth and fifth thoracic vertebrae with resultant scoliosis, the convexity being to the left. There was no definite evidence of osteomyelitis.

Autopsy.—Postmortem examination revealed gram-positive cocci in a staphylococcus formation in fresh vegetations on the aortic and mitral valves. There were miliary abscesses in the lungs, liver, kidneys, spleen, colon and skin, and a recent purulent prostatitis. The body of the fourth thoracic vertebra showed suppuration in its right lateral portion. There was suppuration in the surrounding paravertebral structures and in and about the fourth right costovertebral articulation. No perforation was seen leading from the body of the fourth thoracic vertebra into the epidural space. An extensive epidural abscess was found, apparently secondary to the suppuration in and about the fourth right costovertebral articulation. On October 15, from the epidural abscess yielded Staphylococcus aureus on culture. On October 17, vegetations from the aortic and mitral valves showed gram-positive cocci in staphylococcus formation.

Comment.—This patient had an acute bacterial endocarditis, most probably secondary to squeezing a furuncle of the neck, with multiple

metastatic abscesses, one of which was situated in the fourth thoracic vertebra and gave rise to an epidural abscess. Of interest is the following consideration:

It is possible that the localization of bacteria occurred in the body of the fourth thoracic vertebra because of the existence of an old lesion of this bone, as evidenced by the x-ray plate and the sclerosed bone removed at operation, which had given rise to the scoliosis and possibly created a "locus minoris resistentiae."

CASE 16.—A. S., a man, aged 30, was admitted to the hospital on May 30, 1927, with a known history of Hodgkin's disease for two years, for which he had received roentgenotherapy with considerable relief. For two months he had been having increasing weakness and loss of weight with occasional fever. He had difficulty in breathing, and an intranasal operation was performed with some relief. There was also difficulty on urination.

Physical examination showed a markedly emaciated man *in extremis*. No lymph nodes were palpable. Murmurs were heard over the mitral and aortic areas. There was edema of the lower extremities, with evidence of fluid in the peritoneal and pleural cavities.

Course.—The patient died the day after admission, presumably with respiratory paralysis.

Autopsy.—Postmortem examination revealed a man with marked brownish pigmentation of the abdominal skin, edema of both legs, bilateral purulent bronchitis and bilateral pleural empyema. There were widespread Hodgkin's infiltrations in the lungs, liver, spleen, bone and retroperitoneal lymph nodes. There was 2,400 cc. of purulent fluid in the abdomen, secondary, probably, to multiple abscesses in the spleen. The lumbar vertebrae presented red marrow diffusely mottled by a yellowish translucent gray amorphous material. The fourth lumbar vertebra on section showed a broken-down area, the size of a cherry, filled with greenish pus. No bacteriologic studies were made.

Comment.—This case is one of widespread granulomatous disease with resulting cachexia. The widespread superimposed infection which probably arose from the purulent bronchitis, affecting especially the areas of Hodgkin's infiltrations, masked the presence of an abscess in a lumbar vertebra. In this case the latter was clinically insignificant.

ADDENDUM

Since the submission of this paper, two additional patients with vertebral osteomyelitis have been admitted to the hospital. One, a girl aged 14 years, suffered a metastatic infection of the fourth lumbar vertebra, secondary to a Staphylococcus aureus bacteremia following the squeezing of a boil. Roentgenograms of the spine taken one month after the onset of the disease showed no abnormality; one month later there was narrowing of the intervertebral space between the third and fourth lumbar vertebrae; after another month there was a kyphosis due to destruction and collapse of the fourth lumbar vertebra with almost complete disappearance of the intervertebral space between the

third and fourth lumbar vertebrae and haziness of the intervertebral space between the fourth and fifth lumbar vertebrae.

The other patient, a man of 37, had a Bacillus proteus infection of the urinary tract with Bacillus proteus bacteremia and metastatic infection of the sixth cervical vertebra. Roentgenograms taken about three weeks after the onset of the disease showed narrowing of the intervertebral space between the fifth and sixth cervical vertebrae; five weeks later, roentgenograms showed destruction and collapse of the sixth cervical vertebra.

In each of these cases, roentgenograms afforded evidence confirmatory of the clinical diagnosis of vertebral osteomyelitis. A point worth stressing is that in each case an intervertebral space adjoining the diseased vertebra was definitely narrowed before there was certain abnormality in the appearance of the diseased bone itself.

SPONTANEOUS NONTRAUMATIC PERIRENAL AND RENAL HEMATOMAS

AN EXPERIMENTAL AND CLINICAL STUDY

HUGH J. POLKEY, M.D.
Assistant Professor, Rush Medical College
AND
WILLIAM J. VYNALEK, M.D.
Instructor, Rush Medical College
CHICAGO

A few years ago, during work on a series of experiments on the renal veins, it was observed that marked hemorrhage was frequently associated with venous obstruction of the kidney. In several instances a large perirenal hematoma followed complete ligation of the renal vein. Subcapsular and parenchymal hemorrhages were present constantly in the large, tense, congested kidneys.

It occurred to us that certain cases of spontaneous nontraumatic perirenal hematomas in man might find an explanation in venous congestion of the kidneys, with the resultant elevated vascular pressures and possible capsular ruptures.

We divided our investigations into three kinds of research: (1) the clinical study of a personal case, (2) the experimental ligature of the renal veins in animals and (3) the etiologic study of cases collected from the world's literature.

We believe that elevation of intracapsular and vascular pressure in the kidney can, and probably frequently does, produce spontaneous hemorrhages and even ruptures of the renal capsules with resultant perirenal hematoma. This action would be favored by renal diseases and slight traumas.

By the term "perirenal hematoma" we include subcapsular and extracapsular hematomas and renal and pararenal hemorrhagic cysts. Hemorrhagic renal cysts have been included by so many earlier writers in discussions of perirenal hemorrhage that any complete study of the literature must again include them, unless one attempts a reclassification.

At the German Surgical Congress in 1912, Professor Ritter advised ligature of the renal veins in tuberculosis of the kidneys when nephrectomy was not advisable. He explained that, in animals, ligature of the renal vein produced a long-continued congestion of the kidney. In

the course of from three to five weeks there resulted an atrophy of the kidney by fibrosis, the kidney being reduced to about one third of its normal size. He noticed the production of hemorrhages similar to the forms of perirenal hematomas found in man.

We hope to give some evidence that spontaneous hematoma in man is quite similar in cause and effect to hematoma produced in animals by ligature of the renal vein.

The following is a report of a case of perirenal hemorrhage seen by us, in which the patient recovered following operation, though the causative factor was never demonstrated.

REPORT OF CASE

Complaint.—Mrs. L. P., a white woman, aged 39, began her regular menses on April 30, 1931, and as usual was quite comfortable. At 3:30 a. m. on May 5, she was awakened by a terrific pain in the lower right abdominal quadrant which "felt as though something inside were twisting." She was nauseated and vomited four times following her abrupt awakening at 6 a. m. At 6:30 a. m., she was given a hypodermic of morphine. At that time a large mass was felt in the right side of the abdomen and was thought to be a large ovarian cyst with a twisted pedicle. Menses continued as usual. She was sent to St. Luke's Hospital that morning.

History.—The past history was irrelevant except for a round ligament shortening six years previously.

The family history was unimportant.

Inventory of the various systems likewise gave negative results. There had been no loss of weight, dysuria or hematuria. There was no history of trauma, though the patient had been doing some house cleaning the day before, and had done considerable stretching with her right arm in reaching the ceiling.

Examination.—At the hospital, examination revealed a well nourished, rather obese, white woman, lying quietly in bed, not acutely ill. Slight pallor was present. The head and neck were normal; the lungs were clear; the heart was rapid; the blood pressure was 138 systolic and 92 diastolic. The abdomen was obese and relaxed, and there was a mass the size of a grapefruit just above the level of the umbilicus on the right. Its lower border extended into the pelvis. It was movable, doughy to pressure and moderately tender. The reflexes were normal. A vaginal examination revealed no definite connection with the uterus. The temperature was subnormal; the pulse rate, 90, and the respiratory rate, 20.

Laboratory examination showed: red blood count, 3,840,000; white blood count, 18,300; hemoglobin, 75 per cent. The urine (voided specimen) was amber and acid, with a specific gravity of 1.035; it contained more than 50 mg. of albumin per hundred cubic centimeters, many erythrocytes and from 15 to 20 pus cells per high power field. The Wassermann reaction was negative. Catheterized urine showed no blood.

Roentgen examination by Dr. E. L. Jenkinson revealed a mass in the right side of the abdomen pressing against the cecum and displacing is medially. It obscured the shadow of the right kidney and the lower border of the liver.

Course.—On May 7, the pain became more severe, but the mass was smaller. The red blood count had dropped to 2,760,000; the hemoglobin was

53 per cent; the white blood count was 4,000; the coagulation time was two minutes and thirty seconds, and the bleeding time was three minutes and twenty-five seconds.

Exploratory Laparotomy.—On May 7, a midline incision was made just below and later extended around and above the umbilicus. There was free blood in the peritoneal cavity coming from a rent in the parietal peritoneum overlying a large mass in the right perirenal space. The cecum and ascending colon formed the anteromedial wall of the mass. This extended upward above the site of the kidney and down to the appendical region. It was a large retrocecal hematoma that had just ruptured, accounting for the sudden diminution in the size of the mass. One pint of clotted blood was removed. No fresh bleeding parts could be seen. The uterus, tubes and ovaries were normal. The appendix was absent. The gallbladder and kidney seemed normal. A pack was placed in the bed of the mass, with a stab drain in the loin posteriorly.

Postoperative Course.—Except for a rather distressing period of vomiting on the third day after operation, convalescence was smooth. Forty-eight hours after operation, the pack and drain were removed, but there was at no time any evidence of fresh bleeding. On the twelfth postoperative day a right pyelogram was made and found to be normal. The wound was entirely healed on the fifteenth day after the exploration, and the patient went home. Histologic examination of clots by Dr. Edwin Hirsch revealed only red blood cells.

The actual cause of the bleeding was not determined, nor was the bleeding vessel definitely located. The diagnosis was perirenal hemorrhage with the formation of a retrocecal hematoma. This subsequently perforated into the peritoneal cavity.

HISTORICAL DATA

Spontaneous nontraumatic perirenal hematoma was called "Wunderlich's disease" by Coenen, because, in 1856, Wunderlich was the first to describe the disease fully and give it a proper classification.

However, perirenal hematoma had been reported previously by Bonet, who in 1700 found it in a child suffering with an exanthem. Nebel (1717), Rouppe (1770) and Dourlin (1803) had found spontaneous forms associated with aneurysm of the renal artery. Traumatic forms with aneurysm of the renal artery were reported by Danyau (1835), Mounier (1849) and Hilton (1868). Rayer (1839) observed a case originating in a suprarenal hemorrhage. Dickinson (1883), Malherbe (1890) and Armstrong (1895) saw cases in which there was chronic nephritis. Bellamy (1888) found a renal blood cyst of unknown etiology, probably an old hematoma. Koch, Brin, Judd and Munger described hemorrhagic cysts. Morris (1897) reported a case of unknown cause, associated with carcinoma of the uterus. Parrot (1872) saw 4 cases of suprarenal hemorrhage, in 3 of which thrombosis of the renal veins and subcapsular bleeding occurred. Suprarenal hemorrhage invading the perinephritic tissues was reported by Droubaix (1887), Mattei (1863) and Chiari (1885).

Coenen (1910) collected 13 cases, Seidel (1912) 18, Speese (1913) 21, Baggerd (1914) 28, Lincoln (1918) 15, Rapin (1919) 28, Vogeler (1922) 29, Greco (1925) 62 and Mackenzie (1930) 66.

EXPERIMENTS ON DOGS

Under ether anesthesia, 22 dogs were operated on. An oblique left lumbar incision was made, the kidney exposed extraperitoneally, and the renal vein ligated with no. 6 black silk thread. Careful hemostasis was assured.

Of the 22 animals, 5 died, 2 of peritonitis, 1 of massive perirenal hemorrhage, 1 of an infected perirenal hematoma and 1 of distemper. Autopsies disclosed that perirenal hematomas were present in 2 of the 5 and some form of renal bleeding in all. Controls without ligation of the renal vein showed no such perirenal bleeding.

The remaining 17 dogs were killed at varying periods of time. Of these, 14 animals showed perirenal hematomas of various sizes. Some hematomas were large, even completely surrounding the kidney; others were small, usually located below the inferior pole of the kidney. Yet other hematomas were subcapsular. All animals presented parenchymal bleeding, and a few had blood clots in the renal pelvis.

Subcapsular hemorrhages occurred in 33.3 per cent and extracapsular hematomas in 42.8 per cent, a total for both of 76.1 per cent. Twenty-three and three-tenths per cent did not show either subcapsular or extrarenal bleeding, but did show parenchymal hemorrhages. Bleeding into the renal tissue was always present. Capsular rupture occurred in all extracapsular hemorrhages (42.8 per cent).

We conclude, then, from our experimental evidence that spontaneous perirenal bleeding is frequent in complete venous congestion produced by ligature of the renal vein.

PROTOCOLS

Dog 1.—This animal died of peritonitis in twenty-four hours, and no hematoma had occurred.

Dog 7.—This dog died of peritonitis on the third day, and no hematoma had occurred.

Dogs 13 and 14.—These dogs were killed on the third day, and large perirenal hematomas were found. The kidney and hematoma weighed 198 Gm. in dog 13 and 82 Gm. in dog 14. The opposite kidneys seemed normal, weighing 38 and 26 Gm., respectively. The kidneys operated on were large, tense, violaceous and hemorrhagic, with ruptured capsules.

Dogs 15 and 16.—These animals were killed on the fifth day. Dog 15 showed a large perirenal hematoma and dog 16 a marked subcapsular and parenchymal bleeding. In dog 15, the kidney operated on weighed 117 Gm., and that in dog 16,

50 Gm.; the opposite kidneys weighed 40 and 38 Gm., respectively. Rupture of the renal capsule was seen in dog 15.

Dogs 11 and 12.—These animals were killed on the seventh day, and dog 8 died on the same day (of sepsis); all showed perirenal hematomas. The hematoma was large (weight not taken) and infected in dog 8, and rupture of the capsule could be seen. The hematoma was small in dog 11, although the renal mass weighed 206 Gm., against 42 Gm. on the opposite side. The excessive size and weight were due to parenchymal and subcapsular bleeding. The hematoma and subcapsular bleeding were slight in dog 20, the kidney operated on weighing 68 Gm.; the healthy kidney weighed 34 Gm.

Dogs 3 and 10.—These dogs were killed on the eighth day. Both showed renal and some subcapsular hemorrhage, but no perirenal hemorrhage. In dog 10 the kidneys weighed 28 and 26 Gm., respectively, and appeared somewhat congested, with small hemorrhages in the parenchyma. The collateral circulation was not larger than usual.

Dog 2.—This dog was killed on the eleventh day. There was considerable subcapsular and parenchymal hemorrhage, but no extracapsular hemorrhage. (The weights were not taken.)

Dogs 5 and 6.—These animals were killed on the thirteenth day. Dog 5 had subcapsular hemorrhages, but no extracapsular hemorrhage; the kidney operated on weighed 24 Gm. and was firm and sclerotic. Dog 6 showed only small renal hemorrhages, but no subcapsular or extracapsular hemorrhage. The kidney operated on was small, firm and sclerotic and weighed 12 Gm. It evidently was undergoing atrophy by fibrous changes.

Dog 9.—This dog was killed on the fifteenth day. Pyelonephritis and suppurating perirenal hematoma were found on the side on which operation was performed. The kidney operated on weighed 62 Gm., as against the one not operated on, 28 Gm.

Dog 4.—This animal was killed on the twentieth day. Subcapsular and parenchymal hemorrhages were found. The kidney operated on was half normal size, weighing 15 Gm., and was atrophic and sclerotic to gross examination. Dog 21 died of distemper on the twentieth day, but autopsy was not obtained.

Dog 22.—This animal was killed on the twenty-fifth day. A small encapsulated perirenal hematoma lay below the inferior pole of the kidney operated on. The kidney was sclerotic and atrophic and weighed 12 Gm. The opposite kidney was normal in appearance and weighed 24 Gm.

Dogs 17, 18, 19 and 20.—These dogs were killed on the thirty-third day. In dog 17, the kidneys operated on had a curious appearance. It was calcified throughout and had incrustations in the renal pelvis. No intrarenal, subcapsular or perirenal hemorrhages were present. The kidney weighed 16 Gm. The opposite kidney was healthy and weighed 52 Gm. Dog 18 had a perirenal hematoma below the lower pole of the kidney operated on, which was small (18 Gm.). The kidney not operated on weighed 32 Gm. and was quite healthy.

Dogs 19 and 20 showed subcapsular and parenchymal bleeding, but no massive hematomas. The kidney operated on in dog 19 weighed 34 Gm. and the opposite one, 30 Gm. The kidney operated on in dog 20 weighed 8 Gm. and was markedly atrophic and sclerotic. The other kidney, which was not operated on, weighed 36 Gm. and appeared normal.

Of the 5 operative deaths, 1 dog died of distemper, an intercurrent malady entirely outside of our investigations. So we must figure that 4 of our 21 dogs died (19 per cent). One bled to death (4.76 per cent). Three were infected (14.2 per cent).

Atrophy and a reduction in size of the kidneys operated on occurred in 6 cases (28.57 per cent), the atrophy becoming apparent after the second week. The kidney not operated on showed no change.

The histology of the calcified kidney showed an almost complete sclerosis of the cortex, although many tubules and glomeruli still persisted. Numerous small calculi were distributed throughout the renal

TABLE 1.—*Ligation of Renal Veins in Dogs* *

Dog	Duration of Life, Days	Hematoma	Weight of Kidney Operated On, Gm.	Weight of Opposite Kidney, Gm.	Results
1	1	None	..	..	Died of peritonitis
2	11	Subcapsular	..	..	Killed
3	8	Subcapsular	..	..	Died of hemorrhage
4	20	Subcapsular	15	..	Killed
5	13	Subcapsular	24	..	Killed
6	13	None	12	26	Killed
7	3	None	..	..	Died of peritonitis
8	7	Perirenal	..	..	Died of sepsis
9	15	Perirenal	62	28	Killed; infected hematoma
10	8	None	28	26	Killed; hematoma
11	7	Perirenal	206	42	Killed; hematoma
12	7	Perirenal	68	34	Killed; hematoma
13	3	Perirenal	198	38	Killed; hematoma
14	3	Perirenal	82	26	Killed; hematoma
15	5	Perirenal	117	40	Killed; hematoma
16	5	Subcapsular	50	38	Killed; hematoma
17	33	None; calcified kidney	16	52	Killed; hematoma
18	33	Perirenal	18	32	Killed; hematoma
19	33	Subcapsular	34	30	Killed; hematoma
20	33	Subcapsular	8	36	Killed; hematoma
21	20	No examination	..	..	Died of distemper
22	25	Perirenal	12	24	Killed

* Died 5 (22.7 per cent); subcapsular 7 (33.3 per cent); hematoma 76 per cent; perirenal 9 (42.8 per cent); no hematoma 5 (23.8 per cent).

parenchyma, mostly in the cortex. Some incrustations adhered to the renal pelvis also.

REVIEW OF THE LITERATURE

A review of the literature yielded 178 cases of spontaneous nontraumatic perirenal hematomas. A few additional cases mentioned by various authors were not included because the articles describing them were not available and the details were unobtainable. Such were the cases reported by Dumreicher, Güterbock, Miller, Friedler, Ponfick, Pritchard, Rosenburg, Rose, Schmorl, Turco, Traube, Wildbolz, Yoshikama and Zeno. Some of these may be true cases of perirenal hematoma. In others the details were too few, or were entirely lacking, as in the cases of Rose and Dumreicher, reported by Etcheverry. In

the traumatic forms described by Danyau, Gruber and Rouppe spontaneous bleeding developed long after the trauma, so may be considered in our list as spontaneous ruptures. Marshall's case was traumatic also, but is included as an infected hematoma. The cases reported by Hogge, Bilschai and Parrot were short of details, but we believe that they should be included. Of the hemorrhagic cysts reported by Etcheverry, the cases of Piorry, Bellamy, von Brackel and Recamier should be included. Recently Munger reported 19 cases of acute hemorrhagic cysts of the kidneys, which probably belong here as parenchymal or subcapsular hematomas. To our cases he added those of Siredey, Lancereaux, Maisonneuve, Poirier, Guiliani, Begg, the Mayo Clinic (2 cases), Wolff (2 cases), Roussel and his own. Of the suprarenal hemorrhages reported by Droubaix, the cases of Rayer, Droubaix and

TABLE 2.—*Ages*

Years	Number of Cases
0 to 10	4
11 to 20	12
21 to 30	25
31 to 40	38
41 to 50	34
51 to 60	27
61 to 70	11
71 to 80	1
81 to 90	2
Old man	1
No record	22
Total	178

Chiari may be considered. Actually, we have assembled 200 cases, only 178 of which were analyzed.

Age.—The ages in the 178 cases ranged from 6 days to 89 years. In 70 per cent of the cases the ages ranged from 20 to 60 years, and in 40 per cent, from 30 to 50 years. Thus hematoma is seen to occur most frequently during active adult life and rarely in the extremes of life.

Sex.—Males were attacked more often than females: males 91; females 64; not recorded 23. A ratio of 3:2 obtains. In some articles the ratio was 2:1.

Conditions.—Subcapsular hematomas, including blood cysts, occurred in 37 of 200 cases, or 18.5 per cent, and extrarenal hematomas in 163 cases, or 81.5 per cent. Parenchymal bleeding is recorded in nearly every case examined histologically. Renal blood cysts are mentioned in 23 cases (11 per cent), pararenal blood cysts in 6 (3 per cent) and hematonephrosis in 8 (4 per cent).

Our experimental work showed parenchymal bleeding in all cases. The extrarenal hematomas varied in size from small blood clots just below the lower pole to extensive perirenal masses completely surrounding the kidney. The subcapsular bleeding varied likewise from multiple petechiae under the capsule to large subcapsular blood masses. A complete hematonephrosis or true hematic renal cysts were not obtained in this series.

Subcapsular hematomas were recognized in 7 dogs, or 33.3 per cent, of our 21 animals, and extrarenal hematomas in 9, or 42.8 per cent. Thus perirenal hematoma occurred in 76 per cent of our experiments on animals and parenchymal bleeding in all (100 per cent).

The causes of perirenal hematomas suggested by various authors are numerous. The cause in certain instances was definite, while in others

TABLE 3.—*Renal Conditions Alone as Registered in Our 178 Cases*

Conditions	Cases	
Nephritis	30	
Renal tumors	22	
Aneurysm of renal artery	20	
Arteriosclerosis	12	
Hydronephrosis	7	
Periarteritis	7	
Renal tuberculosis	4	
Renal lithiasis	3	
Cystic kidney	3	
Erosion of renal artery	2	
Thrombosis of renal vein	1	
Renal congestion (prostatism)	1	
Total cases	112 or 63%	69%
Suprarenal conditions	11 or 6%	

it was suggested by the associated pathologic changes. The causes may be divided into 7 groups, as follows:

1. Trauma is the most frequent cause. It is not considered in this article.

2. Diseases of the kidneys were causative in 112, or 63 per cent of 178 cases, and included, in the order of frequency, nephritis, tumors, hydronephrosis, infections, tuberculosis, lithiasis, cystic disease, etc. Diseases of the suprarenals occurred in 11, or 6 per cent of the analyzed cases; diseases of the kidneys and suprarenals together comprised 69 per cent of the cases.

3. Diseases of the blood vessels occurred as causative factors in 29.2 per cent, and as associated pathologic processes in 36 per cent of our 178 cases. Included here were arteriosclerosis, aneurysms, periarteritis nodosa, infarcts and thrombosis.

4. Diseases of the blood were incriminated in 4.5 per cent of our 178 cases. Included were hemophilia, polycythemia, leukemia, scurvy, purpura and Hodgkin's disease.

5. Infections were located as causative in 10 per cent and as the pathologic change present in 13.4 per cent of our cases. The infections were renal, extrarenal and general, and included the following: renal tuberculosis, sepsis, appendicitis, prostatitis, pyelonephritis, perinephritis, scarlatina, malaria, typhoid fever, syphilis and pyemia.

6. Diseases of the retroperitoneal tissues occurred in a few cases. Such were perinephritis, erosion of the arteries, embolism, thrombosis, suprarenal hemorrhages and aortic diseases.

7. No cause was given in 26 cases, or 14.6 per cent.

Renal congestion and hypertension can and do occur in nearly all these conditions, and are particularly prone to appear in nephritis, arteriosclerosis, hydronephrosis, periarteritis nodosa, lithiasis, cystic kidney, thrombosis of the renal vein and prostatism. Clinically, then, we may conclude that congestion and renal hypertension may occur more or less often and be a factor in the causation of bleeding and perhaps rupture of the kidney, especially when associated with pathologic conditions.

PATHOLOGIC ANATOMY

Whatever the cause may be, the renal hemorrhage is always parenchymal; it may remain subcapsular or become perirenal, and it varies from small ecchymoses to large hematomas.

The renal hemorrhage is usually acute and extends rapidly and progressively in all directions, mostly downward toward the iliac fossa, into the mesentery and along the large abdominal vessels. Hematuria may or may not be present. The usual course is progressively downward, with a tendency toward exsanguination.

The pressure in the hematoma may eventually equal the arterial pressure, and clotting may stop the hemorrhage, with a tendency toward recovery.

Rarely the hematoma may migrate and rupture into the peritoneal cavity or into any of the abdominal viscera.

The hemorrhage may resorb more or less completely, and cure may be established spontaneously by resolution. It may organize into a mass of firm fibrosis. It may become encapsulated by fibrous tissue or undergo central degeneration and absorption with the eventual formation of renal or pararenal cysts. It may be infected by direct extension of inflammations from the kidney or adjacent organs or by a blood-borne infection.

Large subcapsular hemorrhages will at times denude the entire kidney of its capsule to form a good-sized cyst in which the kidney lies, either as a healthy or as a more or less degenerated organ. Legueu reported cases of this kind and designated them "hemato-nephrosis."

Smaller subcapsular and parenchymal hematomas may form a type of hemorrhagic renal cyst.

Cases of hematonephrosis were reported by Kirmisson, Legueu, Fowler, Krogius, Baló and Connerth.

Hemorrhagic cysts of the kidney were reported by Amberger, Cibert, Körte, Gouget and Souligoux, Piorry, Recamier, Lancereaux, Wolff, von Brackel, Armstrong, Guiliani, Begg, Maisonneuve, Mayo, Munger, Poirier, Roussel and Siredey.

Extrarenal blood cysts were reported by Bellamy, Leopold, Malherbe, Picqué, Walther, Minkowski, Friedrich, Lippens, Fedoroff, Hullsiek and Sohn. They may or may not connect with the kidney.

Old organized sclerotic hematomas were reported by Gyselynck and by Kümmel.

Infected hematomas occurred in the cases of Marshall, Michaux, Körte and Floyd and Pittman, perinephritis being the diagnosis in the cases of Schultze, Peters, Baló and Sturm. General sepsis as well occurred in the cases of Brunner and Heilmann. Grasmann recorded a septic infarct; Joseph, a suppurative nephritis, and Pauchet, Meyer, Lediard and Meyer and Singer, cases of infected kidneys.

The infections were both general and local and were found to be causative as well as complications. They had a tendency to favor congestions of the kidneys with resultant edemas and elevated renal and vascular tensions. Infections seemed to favor renal hemorrhages and capsular ruptures. It was for this reason that the cases of infected hematomas of Marshall and others were included.

Rupture of the renal capsule was mentioned in 30 cases (16.9 per cent) as follows: Azzurrini, Amberger, Armstrong, Babitzki, Baló, Boland, Bevacqua, Baxter, Cibert, Dickinson, Fedoroff, Floyd and Pittman, Doll, Fowler, Le Clerc-Dandoy, Lenk, Läwen, Hueter, Hullsiek, Hinz, Ilyin, Janssen, LeComte, Meyer, Mertens, Prym, Rosenbach, Schiffmann, Speese, Secrétan and Thomas.

As to the frequency of renal rupture as found at autopsy, we may mention that Küster found it in 0.12 per cent of 7,741 necropsies; Herzog in 16 or 7,805 autopsies, and Güterbock in 10 per cent of 326 autopsies. Henline found 25 cases of spontaneously ruptured kidney in the literature in 1924. Lepoutre assembled 10 cases of ruptured hydronephrosis in 1928.

Hullsiek (1931) computed the number of nontraumatic ruptures of the kidney at 30.

The tendency to rupture is much greater in a diseased than in a healthy kidney. This is especially true in chronic conditions, such as nephritis, arteriosclerosis, lithiasis, hydronephrosis, tuberculosis, neo-

plasms and polycystic disease. Although it is admitted that various forms of trauma, even mild, may be the chief causes of rupture, nevertheless, sudden congestions with elevated intrarenal pressure may play an important rôle in the mechanism of this rupture.

If we accept Tuffier's classification of renal rupture, as ecchymosis, subcapsular rupture and total rupture, then congestions, especially acute types, will assume particular importance (1892).

The cardinal symptoms of the commonly seen acute forms are sudden, sharp, severe pain in the region of the kidney; an abdominal retroperitoneal tumor felt below the costal margin, which rapidly and progressively increases in size, and the signs of internal hemorrhage: such as shock, marked anemia, pallor, cold sweats, clammy skin, prostration, subnormal temperature, low red cell count and low hemoglobin.

In the early stages, or in the forms with an insidious course, only one, or indeed none, of these cardinal symptoms may be present. The later appearance of severe secondary anemia and abdominal tumor or dulness should clear up the doubtful diagnosis in such cases.

The hemoglobin may be quite low, but rarely sinks below 45. The hemoglobin ranged from 45 to 80 in most of our cases. The red cell count is rarely below 3,000,000.

In the absence of a tumor, a dulness in the flank may be elicited at times. The first symptom is almost invariably pain, and tumor soon follows as a close second.

Many cases show gastro-intestinal disturbances, such as nausea, vomiting, meteorism, constipation and ileus. These symptoms are much more marked in the presence of trauma.

The temperature is subnormal at first, but later rises, due to the absorption of fibrin or to infection.

Rigidity of the muscles about the costovertebral angle and upper part of the abdomen is often present, and is more marked when infection ensues or in renal disease.

Hematuria and evidences of nephritis in the urine are frequent findings. Our records show mention of nephritis in 30, or 16.8 per cent. Coenen found pathologic urine in more than 53 per cent. Urinary disturbances are not infrequent, being present as a sign of renal or bladder diseases. Chills, fever and pyuria occur only with associated urinary infections or secondarily infected hematomas. Calculi are occasionally discovered by the roentgenogram.

Lumbar swelling and ecchymosis on the skin rarely appear and are pathognomonic of deep lumbar and perirenal disease.

Exploratory puncture may assist, but usually it fails to clear the diagnosis, since only bloody fluid is obtained.

The tumor was unilateral in 105 cases, 46 on the right and 59 on the left. Six cases were bilateral.

The course was acute and rapidly progressive in the typical severe cases. The chronic forms with slow insidious course and of long duration were described by Cathelin, Lenk and Koch. Such, however, are not frequent. Ordinarily the hemorrhage is progressive, and the tumor grows steadily from day to day. The pain continues severe. The duration of the severe cases is necessarily quite short and varies considerably. Table 4 records the duration of some of the cases to the time of operation or death.

Death may be due to secondary anemia, the result of massive hemorrhage. Other conditions that may be fatal are ileus, pneumonia, peritonitis, sepsis, uremia or operative shock.

The condition has been diagnosed correctly in only a few cases. It is usually confused with the causes of acute conditions within the

TABLE 4.—*Duration of the Disease*

Case	Duration	Case	Duration
Rapin	12 hours	Doll	5 days
Prym	24 hours	Lenk	6 days
Schlichting	24 hours	Pauchet	9 days
Tuffier	24 hours	Michaux	10 days
Waegner	24 hours	Joseph	12 days
Seidel	24 hours	Läwen	13 days
Mackenzie	28½ hours	Hildebrand	3 weeks
Pick	2 days	Minkowski	6 weeks
Oestreich	3 days	Cathelin	3 months
Schäfer	4 days	Koch	1 year
Lediard	4 days	Lenk	1 year

abdomen. It must be differentiated from hydronephrosis, renal lithiasis or tumor, paranephritic abscess, aneurysm of the renal artery, appendicitis, ruptured gallbladder or gastro-intestinal ulcers, torsion of an ovarian cyst, ruptured ectopic pregnancy, etc.

The cardinal symptoms of renal pain, abdominal tumor and signs of internal hemorrhage should furnish a definitive diagnosis in favorable cases.

The prognosis is dependent to some extent on the origin of the bleeding, its cause and the kind of treatment given, as well as on the general condition of the patient. It is bad in cases in which treatment is not given and in cases with severe renal pathologic changes or a ruptured aneurysm. It is favorable after early nephrectomy and in congestive forms. Severe cases tend toward death.

TREATMENT

The treatment in 47 cases was conservative and expectant and resulted in a mortality of 100 per cent. All authors reported death in

all cases in which treatment was not given: Coenen, Greco, Israel, Rapin, Speese, Seidel, Tschmarke, Abbetti, Babitzki, Bonthius, Mackenzie, Meyer and Singer, Vogeler and others.

Conservative surgical procedures, consisting of the evacuation of blood clots, tamponage and drainage, gave better results. In 43 cases in which the patients were so treated there was a mortality of 40 per cent.

Surgeons soon learned that the kidney was often at fault, and that nephrectomy gave the best results. Sixty-two patients were nephrectomized, with a mortality of 24 per cent.

Of the 174 patients, 98 died (56.35 per cent) and 76 were cured (43.65 per cent).

TABLE 5.—*Results of Treatment in 178 Cases*

	Cases	Cured	Died	Mortality, Percentage
Nephrectomy	62	47	15	24.3
Drainage	43	26	17	40.0
Laparotomy	8	2	6	75.0
Operation	6	1	5	83.0
Hysterectomy	2	0	2	100.0
Decapsulation	1	0	1	100.0
Aspiration	1	0	1	100.0
Herniotomy	1	0	1	100.0
Appendectomy	1	0	1	100.0
Exploratory	1	0	1	100.0
Cholecystectomy	1	0	1	100.0
No operation	47	0	47	100.0
Grand total	174	76	98	
No records	4			
Final total	178	43.65%	56.35%	

Greco assembled 60 cases, in 40 of which the patients were operated on, with cure in 28; 62 per cent by incision and 83 per cent by nephrectomy. The total mortality was 53.3 per cent.

Seidel reported 18 cases, with a mortality of 41.7 per cent for the 12 cases in which the patients were operated on.

Israel showed a total mortality of 60 per cent, Rapin 50 per cent, Meyer and Singer 60 per cent and Speese 47.5 per cent.

Tschmarke collected 38 cases; in 27 of these operations were performed within twenty-four hours; 13 patients were cured (48 per cent), and 14 died (52 per cent). The remaining 11 patients were operated on late, after a lapse of several weeks, and only 1 died (9 per cent). We might inquire how many of the 27 patients who were operated on early would have lived for several weeks without treatment.

Nephrectomy is the operation of choice, unless a bleeding vessel can be caught and ligated, as in cases with extrarenal etiology.

TABLE 6.—*Cases Collected from the Literature* *

Author	Year	Sex; Age	Location	Cause and Pathologic Condition	Treatment	Result
Abbetti	1912	F, 49	Subcapsular	Arteriosclerosis	Nephrectomy	Cured
Amberger	1926	M, 36	Extrarenal	No cause; nephritis; arteriosclerosis; cystic kidney	Nephrectomy	Cured
Armstrong	1895	M, 50	Extrarenal	Nephritis and renal cavity as cause (cyst); aneurysm of renal artery	None	Died
Azzurrini	1912	F, 36	Extrarenal	Nephritis	Hysterectomy	Died
Babitzki	1912	F, 36	Extrarenal	Hydronephrosis	Nephrectomy	Cured
Barnard	1900	Little girl	Extrarenal	Aneurysm of renal artery	None	Died
Baggerd	1914	M, 44	Extrarenal	Hydronephrosis as cause; nephritis	Nephrectomy	Died
Barthels	1930	F, 51	Extrarenal	Suprarenal	Decapsulation of kidney	Died
Bazy	1905	M, old	Extrarenal	Nephritis	Drainage	Died
Baxter	1921	F, 15	Extrarenal	Nephritis as cause	Laparotomy	Cured
Bevacqua	1914	M, 37	Extrarenal	Nephritis as cause; arteriosclerosis; miliary aneurysms	None	Died
von Beck	1912	.....	Subcapsular	No cause	Nephrectomy; nephrotomy	Cured
Boland	1923	F, 51	Extrarenal	Sarcoma of kidney	Nephrectomy	Cured
Bonthius	1931	F, 55	Extrarenal	No cause; suprarenal suspected	Nephrectomy	Cured
Bellamy	1888	F, 44	Subcapsular	No cause; renal blood cyst	Nephrectomy	Died
Bollag	1920	M, 21	Extrarenal	Hemophilia	Drainage	Died
Breitner	1923	F, 22	Extrarenal	No cause; suprarenal ruptured	Drainage	Died
Brunner	1927	M, 41	Extrarenal	Sepsis as cause	None	Died
Brunner	1927	F, 55	Extrarenal	Suprarenal hemorrhage	Drainage	Died
Baló	1925	M, 38	Extrarenal	Hypernephroma	Nephrectomy	Cured
Baló	1925	M, 13	Subcapsular	Nephritis	Nephrectomy	Cured
Baló	1925	M, 78	Subcapsular	Hydronephrosis as cause; arteriosclerosis	None	Died
Baló	1925	F, 44	Subcapsular	No cause; hematonephrosis	Nephrectomy	Cured
Baló	1925	F, 55	Extrarenal	Hydronephrosis and arteriosclerosis as causes; carcinoma of uterus	Laparotomy	Died
Baló	1925	F, 18	Extrarenal	Aneurysm of spermatic artery ruptured	Herniotomy	Died
Baló	1925	F, 26	Extrarenal	Aortic aneurysm	Appendectomy	Died
Baló	1925	M, 56	Extrarenal	Aortic aneurysm	None	Died
Baló	1925	M, 23	Extrarenal	Hemophilia cause; perinephritis	Aspiration	Died
Bilschai	1928	.....	Extrarenal	Toxic nephritis		
von Brackel	1899	M, 18	Subcapsular	Blood cyst of kidney	Resection	Cured
Begg	1926	M, 33	Subcapsular	Blood cyst of kidney	Nephrectomy	Cured
Cathelin	1907	F, 25	Subcapsular	Tuberculosis of kidney	Nephrectomy	Cured
Cathelin	1907	.....	.....	Tuberculosis of kidney		
Chauvin	1930	M, 41	Extrarenal	Epithelioma of ureter	Nephrectomy	Died
Chauvenet	1928	F, 59	Extrarenal	None	Drainage	Died
Cibert	1928	.....	Extrarenal	Cyst of kidney	Nephrectomy	Cured
Coenen	1910	M, 33	Extrarenal	Hemophilia as cause; nephritis	Nephrectomy	Died
Connerth	1923	M, 20	Extrarenal	Hydronephrosis; old hematonephrosis	None	Died
Cordier	1910	M, 60	Bilateral extrarenal	Suprarenal hemorrhage	None	Died
Chisholm	1926	F, 28	Extrarenal	Aneurysm of renal artery	Laparotomy	Died
Danyau	1835	M, 15	Extrarenal	Aneurysm of renal artery; trauma 1 month before	None	Died
Dickinson	1883	.....	Extrarenal	Nephritis	None	Died
Doll	1907	M, 60	Extrarenal	Arteriosclerosis cause; nephritis	No operation	Died
Doll	1907	M, 41	Extrarenal	Arteriosclerosis cause	No operation	Died

* Additional cases (Wunderlich, Wildbolz, Traube, Turco, Schmorl, Pritchard, Ponfick, Miller and Israel) are mentioned in the literature, but we were unable to find details.

TABLE 6.—*Cases Collected from the Literature*—Continued*

Author	Year	Sex; Age	Location	Cause and Pathologic Condition	Treatment	Result
Donati	1924	M, 55	Extrarenal	No record	Operation	Cured
Droubaix	1887	F, 62	Extrarenal	Suprarenal	None	Died
Dorendorf	1927	M, 46	Extrarenal	Arteriosclerosis cause; aneurysm of renal artery	None	Died
Dourlin	1803	M, 53	Extrarenal	Aneurysm of renal artery	None	Died
Ecarius	1928	.....	Extrarenal	Hypernephroma	Operation	Died
Ecarius	1928	.....	Extrarenal	Aneurysm of abdominal aorta	Operation	Died
Eigler	1928	M, 67	Extrarenal	Aneurysm of aorta	None	Died
Eigler	1928	M, 54	Extrarenal	Hypernephroma	Laparotomy	Died
Engel	1906	F, 82	Extrarenal	Aneurysm of renal artery; also arteriosclerosis	None	Died
Fedoroff	1923	F, 35	Extrarenal	No cause; pararenal cyst	Drainage	Cured
Fedinec	1929	F, 33	Extrarenal	Suprarenal	Drainage	Died
Fishberg	1923	M, 33	Extrarenal	Periarteritis nodosa	No record	Died
Floyd and Pittman	1931	M, 39	Extrarenal	Calculus and ruptured kidney as cause; perinephritic abscess	Drainage	Cured
Frazier	1908	M, 27	Extrarenal	Tuberculosis of kidney	Drainage	Cured
Franke	1912	M, 39	Extrarenal	Hypernephroma	Nephrectomy	Cured
Friedrich	1906	M, 22	Subcapsular	Polycythemia as cause; pararenal cyst	Drainage	Cured
Fowler	1911	F, 52	Extrarenal	No cause; cavity in kidney (cyst)	Nephrectomy	Cured
Glie	1929	M, 37	Subcapsular	Hemangioma of kidney	Nephrectomy	Cured
Gaál	1930	M, 47	Extrarenal	Leukemia	Operation	Died
Greco	1925	M, 54	Extrarenal	Prostatism and congested kidneys	Drainage	Cured
Greco	1925	F, 43	Extrarenal	Aneurysm of renal artery	Drainage	Died
Grasmann	1923	F, 36	Extrarenal	Septic infarct of kidney	Nephrectomy	Cured
Gruber	1926	M, 39	Extrarenal	Periarteritis nodosa as cause; traumatic aneurysm of renal artery	None	Died
Goldmann	1912	F, 8	Extrarenal	Sarcoma of kidney	Nephrectomy	Cured
Gouget and Souligoux	1905	F, 16	Extrarenal	Renal blood cyst as cause	Nephrectomy	Died
Gutiérrez	1928	F, 34	Extrarenal	No cause	Drainage	Cured
Gyselynck	1910	.....	Extrarenal	No cause; old organized hematoma		
Giuliani	1913	F, 52	Subcapsular	Blood cyst of kidney	Nephrectomy	Cured
Harris and Friedrichs	1922	M, 32	Extrarenal	Periarteritis nodosa	None	Died
Hawkins	1894	M, 31	Bilateral extrarenal	Aneurysm of renal artery	None	Died
Haebler	1928	F, 34	Extrarenal	Nephritis cause; scorbutus	Drainage	Cured
Hartmann	1906	.....	Extrarenal	Carcinoma of kidney	Nephrectomy	Cured
Hildebrand	1895	F, 19	Extrarenal	Aneurysm of renal artery	Drainage	Cured
Hering	1912	M, 7	Extrarenal	Scarlatina cause; nephritis	Drainage	Died
Herzberg	1930	F, 89	Extrarenal	Renal tumor	Laparotomy	Died
Higgins (Fulton)	1904	F, 36	Extrarenal	Aneurysm of renal artery	None	Died
Hinz	1913	F, 56	Extrarenal	Myolipoma of kidney	Nephrectomy	Cured
Heilmann	1930	.....	Extrarenal	No cause	Nephrectomy	Cured
Heilmann	1930	M, 56	Extrarenal	Arteriosclerosis	None	Died
Heilmann	1930	M, 27	Extrarenal	Sepsis	Drainage	Cured
Heilmann	1930	F, 14	Extrarenal	Scarlet fever; nephritis	None	Died
Hogge	1920	.....	Subcapsular	No cause		
Hueter	1908	F, 35	Extrarenal	Nephritis	None	Died
Hulisiek	1931	F, 49	Subcapsular	No cause; pararenal cyst	Nephrectomy	Cured
Ilyin (Israel)	1929	F, 38	Extrarenal	Nephritis and adenocarcinoma of kidney	Nephrectomy	Cured
James	1930	F, 36	Extrarenal	Cirrhosis of liver	Drainage	Cured
Janssen	1922	M, 28	Extrarenal	Periarteritis nodosa	Drainage	Died

TABLE 6.—*Cases Collected from the Literature*—Continued*

Author	Year	Sex; Age	Location	Cause and Pathologic Condition	Treatment	Result
Joseph	1908	M, 50	Extrarenal	Suppurative nephritis	Nephrectomy	Died
Joseph	1908	M, 18	Subcapsular	Toxic nephritis	Drainage	Cured
Keen	1900	F, 45	Extrarenal	Aneurysm of renal artery	Nephrectomy	Cured
Kirmisson	1899	F, 12	Subcapsular	No cause; hematonephrosis	Drainage	Cured
Koch	1909	M, 31	Bilateral extrarenal	Pararenal cyst; nephritis	None	Died
Körte	1912	M, 57	Extrarenal	Renal cyst cause; infection	Nephrectomy	Died
Körte	1912	.....	Extrarenal	Sarcoma of kidney	Nephrectomy	Cured
Krogius	1922	F, 67	Subcapsular	No cause; hematonephrosis; cyst; nephritis	Drainage	Cured
Krogius	1922	M, 55	Subcapsular	Nephritis	Drainage	Cured
Kümmell	1914	M, 33	Extrarenal	Nephritis; sclerosed hematoma	Nephrectomy	Cured
Lancereaux	1868	M, 76	Subcapsular	Blood cyst of kidney	None	Died
Laux	1925	M, 47	Extrarenal	Periarteritis nodosa	None	Died
Läwen	1912	M, 20	Extrarenal	Hemophilia	None	Died
Läwen	1922	M, 49	Subcapsular	Calculus; pyelonephritis	Operation	Died
Lenk	1909	F, 20	Extrarenal	Nephritis	Drainage	Died
Lenk	1909	F, 28	Extrarenal	Nephritis cause; hydronephrosis	Nephrectomy	Cured
Leclerc-Dandoy	1909	M, 60	Extrarenal	Nephritis	Nephrectomy	Cured
LeComte	1926	M, 23	Extrarenal	Hydronephrosis	Nephrectomy	Cured
Lejars and Sebileau	1887	F, 49	Extrarenal	Suprarenal cause; renal blood cyst	Exploratory operation	Died
Lediard	1924	F, 49	Subcapsular	Nephritis cause; renal infection	Nephrectomy	Died
Legueu	1902	M, 38	Subcapsular	No cause; hematonephrosis	Nephrectomy	Cured
Leconte	1897	.....	Extrarenal	Suprarenal		
Lehnert	1914	M, 62	Extrarenal	Arteriosclerosis as cause; nephritis	None	Died
Leopold	1882	F, 33	Extrarenal	No cause; blood cyst of kidney	Nephrectomy	Cured
Lippens	1913	F, 58	Extrarenal	Arteriosclerosis and nephritis cause; hematonephrosis	Nephrectomy	Cured
Lincoln	1918	M, 64	Extrarenal	Arteriosclerosis; rupture of renal artery; nephritis	Nephrectomy	Died
Maisonneuve	1865	M, 57	Subcapsular	Blood cyst of kidney	Puncture	Died
Marshall	1883	F, 13	Extrarenal	Suppurative hematoma 9 months after trauma	Drainage	Cured
Mackenzie	1930	M, 35	Extrarenal	Polycythemia	Nephrectomy	Cured
Malherbe	1890	M, 28	Extrarenal	Nephritis; hematonephrosis	Nephrectomy	Cured
Mertens	1922	M, 21	Extrarenal	Periarteritis nodosa	Laparotomy	Died
Meyer	1919	M, 27	Extrarenal	Pyelonephritis; eroded artery	Nephrectomy	Cured
Meyer	1919	M, 42	Extrarenal	Hypernephroma	Drainage	Died
Meyer and Singer	1927	F, 46	Extrarenal	Aneurysm of renal artery; infected renal pedicle	Nephrectomy	Cured
Michaux	1906	M, 46	Extrarenal	Cause: aneurysm of epigastric artery; arteriosclerosis, infection	Drainage	Died
Minkowski	1906	M, 21	Extrarenal	Polycythemia cause; pararenal blood cyst	Drainage	Cured
Morris	1886	F, 38	Extrarenal	No cause; carcinoma of uterus	.....	Died
Mayo Clinic	1927	M, 72	Subcapsular	Blood cyst of kidney	Nephrectomy	Cured
Mayo Clinic	1928	M, 24	Subcapsular	Blood cyst of kidney	Resection	Cured
Markley	1909	M, 70	Extrarenal	Aneurysm of renal artery	None	Died
Miller	....	.....	.....	.....	.....	.....
Munger	1932	F, 54	Subcapsular	Blood cyst of kidney	Nephrectomy	Cured
Nicolich	1930	.....	Extrarenal	Arteriosclerosis cause; thrombosis of renal vein	None	Died

TABLE 6.—*Cases Collected from the Literature*—Continued*

Author	Year	Sex; Age	Location	Cause and Pathologic Condition	Treatment	Result
Oestreich	1891	F, 50	Extrarenal	Aneurysm of renal artery; arteriosclerosis	None	Died
Pauchet	1911	M, 55	Extrarenal	.....	Drainage	Cured
Pauchet	1911	M, 48	Extrarenal	Infected kidney	Drainage	Died
Pick	1910	F, 53	Extrarenal	No cause	Drainage	Cured
Pagenstecher	1912	.....	Extrarenal	Sarcoma of kidney	Nephrectomy	Died
Peters	1921	M, 38	Subcapsular	Perinephritis	Nephrectomy	Cured
Picqué	1898	F, 35	Extrarenal	No cause; pararenal blood cyst	Nephrectomy	Cured
Parrot	1872	.....	Subcapsular	Suprarenal; thrombosis of renal vein	No record	
Parrot	1872	.....	Subcapsular	Suprarenal; thrombosis of renal vein	No record	
Parrot	1872	.....	Subcapsular	Suprarenal; thrombosis of renal vein	No record	
Prym	1924	F, 59	Extrarenal	Hypernephroma	Nephrectomy	Died
Prym	1924	F, 44	Extrarenal	Chorio-epithelioma in kidney from uterus	Hysterectomy	Died
Padtberg	1923	M, 54	Extrarenal	Nephritis	Laparotomy	Died
Piorry	1835	F, 50	Subcapsular	Renal blood cyst	None	Died
Pritchard	....	.....	.....	.....	.....	.....
Ponfick	....	.....	.....	.....	.....	.....
Poirier	1888	F, 48	Subcapsular	Renal blood cyst	Puncture	Died
Rayer	1837	M, 75	Extrarenal	Suprarenal	None	Died
Rayer	1839	M, 65	Extrarenal	Suprarenal	Drainage	Cured
Rapin	1919	M, 35	Extrarenal	Nephritis	Drainage	Died
Recamier	1893	F, 59	Subcapsular	Renal blood cyst	Resection	Cured
Reinhardt	1918	F, 30	Extrarenal	Aneurysm of ovarian artery	None	Died
Reuss	1912	6 days	Extrarenal	Suprarenal	None	Died
Richardson	1925	M, 59	Extrarenal	No cause, aneurysm of renal artery	Nephrectomy	Cured
Richer	1911	M, 42	Extrarenal	Nephritis	None	Died
Ricker	1911	M, 40	Extrarenal	Spinal paralysis; infarct of renal bed as cause	None	Died
Ricker	1911	M, 40	Extrarenal	Gallbladder disease	Cholecystectomy	Died
Rihmer	1916	.....	Extrarenal	Suprarenal cause; typhoid		
Ritter	1912	M, 29	Extrarenal	Suprarenal	Drainage	Died
Rosenbach	1917	M, 32	Extrarenal	Hypernephroma	Nephrectomy	Died
Roth	1924	M, 48	Extrarenal	Nephritis and arteriosclerosis cause	None	Died
Rouppe	1770	.....	Extrarenal	Traumatic aneurysm of renal artery	None	Died
Roussel	....	M, 23	.....	Blood cyst of kidney	Nephrectomy	Died
Saint-Cène	1921	M, 35	Extrarenal	No cause	Nephrectomy	Cured
Schäfer	1921	M, 46	Extrarenal	Arteriosclerosis	Nephrectomy	Died
Szenes	1923	M, 48	Extrarenal	Nephritis and infarct	Nephrectomy	Cured
Schultze	1916	F, 29	Extrarenal	No cause	Drainage	Cured
Schultze	1916	M, 64	Extrarenal	Pyemia; perinephritis	Drainage	Died
Schlichting	1912	M, 28	Extrarenal	Nephritis	Drainage	Cured
Schiffmann	1915	F, 26	Extrarenal	Nephritis	None	Died
Schloss	1926	F, 41	Subcapsular	Tuberculosis of kidney	Nephrectomy	Cured
Seidel	1912	M, 28	Extrarenal	Nephritis	Drainage and laparotomy	Cured
Secrétan	1930	M, 26	Extrarenal	Hydronephrosis	Nephrectomy	Cured
Soroko	1927	M, 34	Extrarenal	Tumor of kidney	Nephrectomy	Cured
Speese	1913	M, 43	Extrarenal	Nephritis	Nephrectomy	Cured
Swan	1931	.....	Extrarenal	Renal adenoma	Nephrectomy	Cured
Sturm	1930	M, 50	Extrarenal	Perinephritis; trauma	Drainage	Cured
Sturm	1930	M, 55	Extrarenal	Perinephritis; trauma	Drainage	Cured
Schramm	1925	F, 50	Extrarenal	Aneurysm of renal artery	None	Died
Sohn	1921	F, 64	Subcapsular	Arteriosclerosis; hematonephrosis	Drainage	Died
Sohn	1921	F, 54	Subcapsular	Arteriosclerosis; hydronephrosis; carcinoma of uterus	None	Died

TABLE 6.—*Cases Collected from the Literature*—Continued*

Author	Year	Sex; Age	Location	Cause and Pathologic Condition	Treatment	Result
Singer	1928	F, 50	Extrarenal	Aneurysm of renal artery; arteriosclerosis	Nephrectomy	Cured
Singer	1928	F, 46	Extrarenal	Infection and erosion of renal artery	Nephrectomy	Cured
Schmorl	....	.....	.....	.....	.....	.....
Schmorl	....	.....	.....	.....	.....	.....
Siredey	1858	M, 38	Subcapsular	Lead poisoning; blood cyst of kidney	None	Died
Tage-Hansen	1918	F, 35	Extrarenal	No cause	Drainage	Cured
Trulli	1916	M, 66	Extrarenal	Aneurysm of renal artery	Operation	Died
Thomas (Judd)	1917	M, 65	Extrarenal	Calcified hydronephrosis	Nephrectomy	Cured
Tschmarke	1929	M, 49	Extrarenal	Metastatic carcinoma of kidney	Nephrectomy	Died
Tuffier	1906	M, 40	Extrarenal	Sarcoma of kidney	Nephrectomy	Died
Turco	1927	.....	.....	.....	.....	.....
Traube	1871	.....	.....	.....	.....	.....
Wolff	....	Young man	Subcapsular	Blood cyst of kidney	Nephrectomy	
Wolff	....	Young man	Subcapsular	Blood cyst of kidney	Nephrectomy	
Vogeler	1922	F, 62	Extrarenal	Aneurysm of renal artery	None	Died
Wade	1915	M, 20	Bilateral extrarenal	Nephritis cause; syphilis and malaria	None	Died
Waegner	1931	M, 39	Extrarenal	Aneurysm of renal artery	Drainage	Died
Walther	1902	F, 22	Extrarenal	No cause; cathartic; pararenal blood cyst	Drainage	Cured
Walter	1921	M, 33	Bilateral extrarenal	Periarteritis nodosa	None	Died
Willis and Bonet	1700	Child	Extrarenal	Exanthem (infection)	None	Died
Wright	1931	F, 70	Extrarenal	Tumor of kidney	Nephrectomy	Cured
Wildbolz	....	.....	.....	.....	.....	.....
Wunderlich	1846	.....	.....	.....	.....	.....
Zweig	1928	M, 46	Extrarenal	Arteriosclerosis	Drainage	Cured

SUMMARY

1. Seventy-six per cent of experiments on animals with ligation of the renal vein were positive for perirenal hematoma, and 100 per cent for parenchymal hemorrhage.

2. One hundred and seventy-eight assembled cases showed almost 70 per cent of renal and suprarenal disease associated with perirenal hematoma.

3. The causative disease of the kidneys, suprarenals, blood vessels and infections are all capable of sudden congestions of the organs and elevation of intrarenal tension.

4. Spontaneous perirenal hematoma may often be the result of sudden congestion of a diseased organ.

5. A case is reported which was due to an extrarenal cause.

6. Nephrectomy is the operation of choice, with renal bleeding.

7. Spontaneous cases in which no cause is discovered are probably explained by a sudden renal congestion, acting on some pathologic condition of the kidney or of the perirenal tissues. Even in the cases with a demonstrable cause, the mechanism of hemorrhage may be as suggested.

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TRANSPLANTATION OF THE INTACT MAMMALIAN HEART

FRANK C. MANN, M.D.
AND
JAMES T. PRIESTLEY, M.D.
ROCHESTER, MINN.
AND
J. MARKOWITZ, M.D.
AND
WALLACE M. YATER, M.D.
WASHINGTON, D. C.

The subject of transplantation of various tissues or organs is important, since great practical value might come from the development of a successful method. This applies particularly to the transplantation of an organ such as the kidney, whereby a normal organ might be exchanged for a diseased one. A comprehensive review of the subject of transplantation of tissue has been made recently by Loeb,[1] and we shall, therefore, mention only a few considerations which are pertinent to our report.

Two methods have been used for the transplantation of tissue. The method usually employed both clinically and experimentally has been to excise a small section of tissue and to implant it in the desired situation, expecting it to obtain its own blood supply. The other method has been to transplant a whole organ, anastomosing its blood vessels to other suitable vessels. The latter method was made technically possible by the development of vascular surgery by Carrel.[2] Owing to the claims of certain surgeons, with particular reference to implantation of sex glands and the striking success of an occasional experimental transplantation, the procedure often is considered successful. However, the results of numerous investigators have demonstrated that autotransplantation, that is, reimplantation of tissue or of an organ in the same subject often is successful, whereas homotransplantation, that is, implantation into another subject of the same species is rarely successful, regardless of the tissue or organ transplanted.

From the Division of Experimental Surgery and Pathology, the Mayo Foundation, and the Physiologic Laboratory of Georgetown University School of Medicine.

1. Loeb, Leo: Transplantation and Individuality, Physiol. Rev. **10**:547 (Oct.) 1930.

2. Carrel, Alexis: The Surgery of Blood Vessels, Bull. Johns Hopkins Hosp. **18**:18 (Jan.) 1907.

In an investigation in which a denervated heart preparation was desirable, one of us (Dr. Markowitz) suggested that a transplanted heart might be employed. This suggestion led to the present investigation, and, although the results have not fully justified our expectations, they seem worthy of presentation as adding further data concerning transplantation of organs and as demonstrating a method that may be of value in research on the heart. It is obvious that all of our transplantations of the heart are homotransplantations. The essential procedure was to establish coronary circulation of the transplanted heart by anastomosing its aorta to a suitable vessel of the recipient. From the results of preliminary experiments which included several methods of procedure, two technical methods were developed which gave about equally successful results. With the first method, it was essential to maintain the tonus of the heart as long as possible throughout the procedure and to establish the coronary circulation by anastomosing the central end of the carotid artery to the aorta. This was accomplished by first preparing the necessary vessels of the recipient and then obtaining the heart from the donor by the judicial ligation of the larger arteries in relation to the ligation of the larger veins so that effective coronary circulation was maintained as long as possible. It was necessary to operate with speed in order to maintain the cardiac tonus and to obviate the possibility of intravascular clotting. It was found possible to transplant a heart in which the time between the cessation of the contraction of the heart and the establishment of the coronary circulation with the blood of the donor was less than five minutes. With the second method, it was essential to ligate the large veins before the large arteries, and thus prevent the possible dilatation of the heart and at the same time stop its contraction. To prevent the possibility of intravascular clotting the donor was heparinized just before operation, and the coronary circulation was established by anastomosis of the aorta to the peripheral end of the carotid artery. The details of the technic follow.

All operative procedures were carried out under ether anesthesia with rigid aseptic technic. The preparation of the field of the recipient was as follows: The carotid artery of one side, preferably the left, and the jugular vein of the opposite side were dissected free. It is convenient, but not essential, to use dogs of good size. The adventitia was carefully stripped from the vessels in the usual manner for anastomosis. The field was then packed off with moist gauze compresses. With a sharp knife these vessels were sectioned between protected clamps from 3 to 4 cm. from the suprasternal notch, and the blood was squeezed out. If the first method of transplantation was to be employed, the peripheral end of the common carotid artery was ligated while the protected clamp was applied to the central end, and the latter was prepared for anastomosis by removal of the remaining adventitia. If the second method of transplantation was to be used, the opposite was done: The peripheral end of the carotid artery was

prepared for anastomosis and the central end ligated. A similar procedure was carried out for the jugular vein, with the difference that the cephalic end of the vein was always tied, the cardiac portion being occluded with forceps. The usual three sutures of fine silk were placed equidistant in each vessel, and the whole field was covered with moist gauze. Meanwhile a small dog was etherized and maintained under artificial respiration.

If the first method of transplantation was carried out, the procedures were as follows: The thoracic cavity was entered through a left intercostal incision, and the heart was exposed. Loose ligatures were placed around the great arteries, aorta, brachiocephalic artery, left brachial artery, vena cava and azygos vein. The pericardium was then entered, and the largest branch of the pulmonary artery was located and tied. The left pulmonary veins were ligated in turn. The right branch of the pulmonary artery and the right pulmonary vein were exposed. Then, in alternate succession, the ligatures were tightened on the aorta and on the other large veins and arteries in such an order that the coronary circulation was maintained, the heart never being allowed to become overdistended. Finally, the remaining pulmonary vessels were ligated. All the vessels were then sectioned distal to the points of ligation, and the heart was removed to the previously prepared operative field of the recipient. The left branch of the pulmonary artery was anastomosed to the previously prepared central end of the right jugular vein. The clamp was removed from the jugular vein, and the blood in the heart gently squeezed out. This not only emptied the heart of blood, but permitted the deposit of fibrin around the suture line, which prevented subsequent leakage. A strong clamp, or if necessary two clamps, were placed 2 to 3 cm. from the line of section of the aorta, and the end of the aorta was prepared for anastomosis. There was no need to remove much adventitia from the aorta. This vessel, especially in young animals, is extremely friable, and should be treated with great care. If the heart was taken from a large dog it was advisable to anastomose the brachiocephalic artery instead of the aorta, as otherwise the disparity in size would be too great.

If the second method of transplantation was to be employed, the thorax and abdomen were opened in the median line. The opening of the abdomen permits freer access to thoracic contents. The incision in the thorax was made in the midsternum; a self-retaining retractor was inserted, and 100 mg. of heparin in 50 cc. of sodium chloride solution, previously boiled, was injected intravenously through the inferior vena cava. This vessel was then promptly tied and cut between ligatures close to the right auricle. The superior vena cava, the azygos vein, the brachiocephalic artery, the left brachial artery and each lobe of the lungs were tied and cut between ligatures. It was essential not to tie the root of the whole lung in one ligature as the ligature almost always slips, causing uncontrollable oozing when the heart begins to beat. A strong forceps was applied to the aorta distal to the left brachial artery, and the heart was removed by cutting this vessel and the diaphragmatic attachment of the pericardium. The pulmonary artery was identified by opening the pericardium over the right auricle, and one of the large branches was carefully freed and transected proximal to its previously placed ligature. The heart was then ready to be sutured to the previously prepared vessels of the host in the manner described. The aorta or the brachiocephalic artery was anastomosed to the peripheral end of the carotid artery, and the pulmonary artery, or a branch of it, to the central end of the jugular vein. As in all anastomoses of veins, care should be taken not to twist the jugular vein while suturing it. Following anastomosis the clamps were removed first from the vein and then from the artery. Blood was permitted

to leak from the latter for a short time in order to make sure that all the air in the length of vessel exposed for anastomosis had been expelled. This prevents coronary embolism due to the entrance of air into the coronary arteries. When it had been accomplished, the clamp was removed from the aorta and a suitable pocket was made for the organ; if the heart beat became established, the wound was closed in the usual manner.

In some experiments the pericardium was removed from the transplanted heart, and in others it was left intact. No particular difference in the length of survival was noted in the two groups of experiments. However, it was found that if the pericardium was also transplanted, a wound should be made to permit the drainage of the large amount of pericardial fluid that always forms.

The main cause for our failures was the distention of the heart with blood before its beat was established. The valves of the heart will not function if the tonus of the cardiac muscle is abolished or low. Since the new pathway for the blood was established only to take care of the coronary circulation, the blood that leaked by the insufficient valves was trapped in the cavities of the quiescent heart. Many different expedients were tried to overcome this difficulty, such as anastomosis of the vena cava of the transplanted heart to the cephalic end of the transected jugular vein, anastomosis of the vena cava to a branch of the pulmonary artery and the making of an artificial foramen ovale. None of these procedures was found to be of sufficient value to merit its employment. The main procedures found to be of value in overcoming this difficulty were: (1) restoration of the coronary circulation by using the peripheral end of the carotid artery, by which method if the pressure was sufficiently low the impaired valves would not leak; (2) temporary opening of one of the venae cava when the quiescent heart began to fill with blood in order to permit the escape of blood until the beat became established, and (3) an attempt to maintain the cardiac tonus so that a minimum of leakage occurred.

GENERAL BEHAVIOR OF THE TRANSPLANTED HEART

The heart usually begins to contract immediately after the coronary circulation is established. Occasionally only the auricles and the right ventricle beat immediately and the left ventricle does not begin to beat until a few hours later. Usually, when the animal has recovered from the anesthetic the pulsations are regular and vigorous. The wall of the right ventricle in its contraction undergoes considerable excursion. The rate of the pulsation varies, but generally on the animal's recovery from the anesthetic it is beating at the rate of from 100 to 130 per minute. In the next twelve hours the rate is surprisingly constant from moment to moment, and extrasystole is not detectable even over long

periods. The pulsations of the transplanted organs do not inconvenience the animal in any way. They can be counted by palpation, or the rate can be recorded with an electrocardiographic apparatus, direct leads from base to apex being employed. The electrocardiographic tracings appear surprisingly normal. If the animal struggles for any reason, the pulsation usually increases. In one experiment the rate rose from 120 to 132, when the animal was prevented from walking across the room. In another experiment the animal was induced to take a vigorous run about the grounds, and the pulse of the transplanted heart increased temporarily about 15 beats per minute.

In several experiments, after careful preliminary observation, the host was given intravenous injections of thyroxin. Within eighteen hours the pulse rate of the transplanted organ was appreciably increased, whereas the rate of the host's own heart was not yet affected. As has been indicated in previous papers,[3] this experiment can be interpreted as demonstrating that the tachycardia following injections of thyroxin is independent of the central nervous system, and that the part that the central nervous system plays is of an inhibitory nature, since the denervated heart was more sensitive to the accelerating influence of this drug.

In general, however, the transplanted heart was found unsuitable for this type of experiment. After from one to eight days, irregularities became apparent which made the accurate determination of the pulse rate impossible. These irregularities were soon followed by absence of pulsation in the transplanted organ or by fibrillation. The longest period of survival in our experience was eight days. The average was about four days. When the heart was removed just before it became quiescent, the left auricle was found to be filled with a clot, and the right auricle and ventricle were distended. The surface of the heart was covered with mottled areas of ecchymosis; the heart was friable on section. Histologically the heart was completely infiltrated with lymphocytes, large mononuclears and polymorphonuclears. In some instances a heart that was beating feebly at the time of removal showed few normal-appearing muscle fibers. Often edema developed around the transplanted heart in the same manner as it occurs around the homotransplanted kidney.

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3. Lewis, J. K., and McEachern, Donald: Persistence of an Accelerated Rate in the Isolated Hearts and Isolated Auricles of Thyrotoxic Rabbits: Response to Iodides, Thyroxine and Epinephrine, Bull. Johns Hopkins Hosp. **48**:228 (April) 1931. Priestley, J. T.; Markowitz, J., and Mann, F. C. The Tachycardia of Experimental Hyperthyroidism, Am. J. Physiol. **98**:357 (Sept.) 1931. Yater, W. M.: The Tachycardia, Time Factor, Survival Period and Seat of Action of Thyroxine in the Perfused Hearts of Thyroxinized Rabbits, Am. J. Physiol. **98**: 338 (Sept.) 1931.

Our observations on the transplanted heart are in general identical with those on other transplanted tissue. It appears that functioning cardiac muscle is no less resistant as a homotransplant than is the similarly transplanted kidney. Even when the heart of a small dog is transplanted into the neck of its mother, the result is the same; the transplanted organ functions well for about twenty-four hours and then becomes irregular, and, as is often the case with the transplanted kidney, function may cease suddenly. The transplanted heart may pulsate with great vigor; five minutes later pulsation may stop completely, and grossly a cause cannot be found to account for it. With regard to short experiments, we have no hesitancy in saying that the transplanted heart should be a valuable test object for the investigation of various physiologic problems. The technic should be looked on as "viviperfusion," the perfusion fluid being unchanged blood and the duration of the perfusion twenty-four hours or more. When the heart has become irregular, it can be removed aseptically without death to the host.

Although occasional failure of the transplanted organ to function was found to be due to intravascular thrombosis, this complication was unusual. As with all other transplanted organs, it was suggested that the failure of the transplanted heart to survive for more than a few days was due to the technic. Although several theoretical considerations make this criticism invalid, nevertheless some experiments were carried out for the primary purpose of minimizing trauma, to determine the length of time the coronary circulation was stopped and for other factors which might have been deleterious to the survival of the transplanted organ. In some of these experiments the heart did not cease beating, and in others it was quiescent for not more than ten minutes. The end-results of these careful experiments were the same, the longest period of survival being five days. When it is borne in mind that there is never any difficulty in preparing an autotransplant of the kidney that will survive in the neck in good condition for months, it is readily seen that the failure of the homotransplanted heart to survive is not due to the technic of transplantation but to some biologic factor which is probably identical to that which prevents survival of other homotransplanted tissues and organs.

SUMMARY

A technic for homotransplantation of the intact mammalian heart was developed. Such transplanted hearts beat vigorously for as long as from one to eight days. However, after about twenty-four hours, irregularities of the beat may develop and the heart may gradually, although sometimes suddenly, cease to function. The general behavior of such a transplanted organ as regards function, period of survival and cytologic changes is similar to that of other homotransplanted organs.

BACTERIOLOGY OF PULMONARY ABSCESS

M. S. MARSHALL, PH.D.
AND
HAROLD BRUNN, M.D.
SAN FRANCISCO

The clinical questions that surround the origin, the diagnosis and the treatment of pulmonary abscess are numerous. A considerable number of them may not be answered in the light of present knowledge of this condition. The answers to some of these practical and pertinent questions must come from the reciprocal orientation of the knowledge of the surgeon and the clinician with the knowledge of the specialist in correlated fields, the roentgenologist, the pathologist, the bacteriologist, and so on. These specialists have their own puzzles. With regard to the bacteriologist, it is perhaps not too much to say that pulmonary abscess, representing a mixed infection that includes a tremendous variety of bacterial types, is extremely puzzling; and it may not be too much to say that few clinical men have been able to keep up with the changing front of bacteriology, and with the status of the great number of organisms that may be found in pulmonary abscess. In fact, few bacteriologists have the right to claim such accomplishment.

In reviewing briefly the work that has been done relative to the bacteriology of pulmonary abscess, and in attempting to show wherein the work that has been done locally agrees or disagrees with reported studies, it will not be possible to touch on some points. It is, however, more important that a bacteriologic concept of the problem be gained, for several years of association with it has revealed clearly that no narrow perspective is adequate.

There are perhaps three questions which the surgeon might ask the bacteriologist, if he did not know that the bacteriologist is not able to answer them. He might first ask whether studies of the bacterial invasion reveal anything with regard to the pathogenesis of the infection. In short, does the original infection come from embolic or from aspiratory processes? He might then ask: Just what organism or organisms are responsible for the original infection, assuming the presence in the advanced abscess of a considerable secondary flora. Coming, then, to

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From the Department of Bacteriology and the Department of Thoracic Surgery, University of California Medical School.

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the progress of the developed case, he might ask in just what way the progress of the disease, and the prognosis, depend on certain particular bacteria or certain groups thereof. The consideration of these questions in their logical order will perhaps constitute a reasonable approach.

The mechanism of infection is a subject concerning which there is considerable argument. Most of these arguments are the result of the idea that the original infection arises from a septic embolus, or that it arises from aspirated blood and mucus from the mouth, presumably under general anesthesia. Cutler and Hunt [1] favor the embolus theory, based on the clinical picture (sudden onset, and so on), the frequency of occurrence in the lower right lobe, the occurrence of metastases to the brain, the frequency following local anesthesia and the frequency following procedures that favor the formation of emboli. A number of cases have occurred on the twelfth day after tonsillectomy, which some consider to favor the embolus theory. Allen [2] indicated from eighty-four cases that 53 per cent followed embolus-producing procedures. There is plenty of evidence, however, showing that foreign bodies, infection of the upper respiratory tract, submersion, and so on, are predisposing factors in many cases.

Bacteriologic evidence with regard to the mechanism of infection arises from two series of observations: There have been many attempts to duplicate the infection in animals, and the study of the bacteria of pulmonary abscess reveals that in type they duplicate closely the flora of the buccal cavity.

The experimental reproduction of abscess of the lung has been accomplished, principally within the last five years, by Smith,[3] Crowe and Scarff,[4] Holman, Weidlein, Cutler and Schlueter,[5] and Joannides,[6] the latter using an admirable series of eighty-seven dogs. Some of these experiments resulted in abscesses of the lungs and a variety of other pulmonary infections, from procedures indicating an embolic origin; similar

1. Cutler, C. C., and Hunt, A. M.: Postoperative Pulmonary Complications, Arch. Int. Med. **29**:449 (April) 1922.

2. Allen, D. S.: Etiology of Abscess of the Lung, Arch. Surg. **16**:179 (Jan.) 1928.

3. Smith, D. T.: Experimental Aspiratory Abscess, Arch. Surg. **14**:231 (Jan.) 1927; Etiology of Primary Bronchiectasis, ibid. **21**:1173 (Dec.) 1930; Fusospirochetal Disease of Lungs Produced with Cultures from Vincent's Angina, J. Infect. Dis. **47**:303 (April) 1930.

4. Crowe, S. J., and Scarff, J. E.: Experimental Abscess of Lung in Dog, Arch. Surg. **16**:176 (Jan.) 1928.

5. (*a*) Holman, E.; Weidlein, I. F., and Schlueter, S. A.: Proc. Soc. Exper. Biol. & Med. **23**:266, 1926. (*b*) Schlueter, S. A.; Weidlein, I. F., and Cutler, E. C.: New York State J. Med. **26**:767, 1926. (*c*) Cutler, E. C., and Schlueter, S. A.: Ann. Surg. **84**:256, 1927.

6. Joannides, M.: Surg., Gynec. & Obst. **47**:449, 1928.

results have been secured by aspiration. Although the experimenter took his individual stand in accordance with the method with which he was most successful, there is nothing to indicate to the outsider that either mechanism is not possible, or even that one is more frequent than the other. From the bacteriologic standpoint, the choice of the dog is unfortunate, owing to the frequency of contaminating flora in the healthy tissues. Furthermore, the artificial production of septic emboli, or the trapping of infected material in the bronchi, has been accomplished with material that does not reveal a clear bacteriologic picture. The most successful experiments have been accomplished by the use of purulent material from a pulmonary abscess as such, by the use of pus from the groin of a guinea-pig previously infected with abscess material, or by the use of material from the buccal cavity, from the tonsils, from pockets of pyorrhea, from lesions of ulcerative stomatitis and the like. Cutler and Schlueter [5c] performed some experiments with bacteriologically specific emboli, and secured fair results with Staphylococcus aureus, Bacterium coli and nonhemolytic streptococci. The pneumococcus failed to induce abscesses. Mr. Goldman, of our group, injected a mixture of Bacillus melaninogenicum and a few contaminating cocci intratracheally into rabbits. The organism named is one described by Oliver and Wherry in 1921; it is a very small, short, gram-negative rod, growing anaerobically on human blood agar, on which it forms a dense black pigment. Varney [7] encountered it in a number of cases of pulmonary abscess; Cohen [8] noted the organism in fourteen of sixteen cases, and we have successfully demonstrated it in more than half the specimens examined. Varney attributed to it the rôle of a significant secondary invader. Its presence in the normal mouth and elsewhere renders somewhat difficult a decision as to its particular significance. Goldman, however, succeeded in inducing a pulmonary infection from which histologic sections gave some evidence of early abscess formation.

That the bacterial flora of material from the well developed abscess is very similar to that of the buccal cavity, particularly of the unhygienic buccal cavity, may be considered as established. Briefly, the flora may consist frequently of fusiform bacilli and spirochetes, of diphtheroids, of B. melaninogenicum, of staphylococci, of all types of streptococci, of organisms of the colon group (B. coli, Proteus vulgaris), of the so-called streptothrices or filamentous types, of Micrococcus tetragenus, of pneumococci, and of gram-negative diplococci of the Neisseria group. Any or all of these may be found in the sputum, together with other organisms less frequently encountered or not easily identified. Any or all

7. Varney, P. L.: Bacterial Flora of Treated and Untreated Abscesses of Lung, Arch. Surg. **19**:1602 (Dec.) 1929.

8. Cohen, J.: Bacteriology of Abscess of Lung and Methods for Its Study, Arch. Surg. **24**:171 (Feb.) 1932.

appear with considerable frequency in specimens from pulmonary abscess. Furthermore, checking the results of our studies of specimens of sputum against the bacteriologic picture of other specimens, it seems probable that the flora of the abscess proper is similar qualitatively to that of the sputum—that is, specimens of sputum even carefully taken reveal a heavy buccal contamination, considered to be contamination for the reason that a bronchoscopic or a surgical specimen reveals similar organisms, but perhaps not so many of some varieties, or it reveals no pneumococci, or no Neisseria. Specimens of sputum should on this basis be avoided whenever possible.

Analysis of the bacteriologic evidence pertinent to the mechanism of infection would seem to indicate that the origin may well be either embolic or aspiratory, and one should probably add the abscess which is induced by pneumonias or other conditions in which it is not possible to be sure that the origin is embolic, lymphatic or otherwise. The flora of pulmonary abscess makes it difficult to picture a septic embolus, particularly, let us say, from a laparotomy, which is contaminated with anything like the organisms found in the advanced stages of the disease. However, it is not necessary to assume that the primary infection is complicated, and it seems virtually unequivocal that the heavy secondary infection which must be postulated arises from the buccal cavity. In other words, not only is it unnecessary to assume either an embolic or an aspiratory origin, but it is somewhat illogical to insist on a single route to the parenchyma of the lung.

In passing on to the next question, it should be pointed out that the two possible approaches to this question as it stands at present seem to be through intimate pathologic study at autopsy and animal experimentation. In the latter, the work which has been done is barely preliminary, and subsequent work, if it is to be enlightening, must be vastly more carefully controlled than has been possible heretofore. Incidentally, speaking as a bacteriologist, it would seem necessary to carry out this approach with better bacteriology than has been the case in most of the experiments that have been performed, at least if any conclusions are to be drawn with regard to the bacteriology of pulmonary abscess.

The question of the specific etiology of pulmonary abscess may be handled briefly. In the literature on the subject, few have ventured to suggest a specific etiologic agent. The suggestions which are made, usually regarding the fusiform bacillus, the spirochetes or a combination of the two, are not made unequivocally. They are speculative opinions. It is possible only to point out the most logical bacteriologic stand in the matter. One may assume that the truly localized abscess, of embolic or bronchiogenic origin, starts with a minor lesion in the parenchyma of the lungs. Presumably this lesion originates as an infection, and at the outset there are no clinical symptoms. Furthermore, it is not possible

to sample the lesion, provided its presence and location were known. Considering the number of suppurative conditions and the number of pyogenic organisms—considering, for a specific example, the number of organisms that may be responsible for various pneumonias—there seems to be no reason for supposing that any one organism is invariably responsible for pulmonary abscess. It is most logical to assume that a number of organisms, singly or in combination, may be responsible for the original infection. It seems virtually impossible to approach this matter seeking a plausible answer except under the rare circumstances in which a pathologically proved abscess is noted and studied immediately after death, an abscess that is in its very early stages. To be sure, the development of the early abscess may be in part determined by the nature of the original infection; it will also be determined by the location and many other factors. Thus, with regard to the specific bacteriology of this question, three points might be emphasized: First, discussions with regard to the specific initial infection rest on very uncertain data; second, the most logical assumption or postulate is that a number of organisms may be involved, not the same in different cases, and third, since the clinical abscess represents an advanced stage, heavily infested with secondary invaders, it is probable that the original infecting agent has no clinical significance.

With regard to the third bacteriologic question, concerning the relationship of the clinical development of pulmonary abscess to the bacteriology, it is likely that much more will be said in the next few years. It is clear that the unsolved clinical questions are numerous. The most casual bacteriologic study reveals that the bacteriology of the disease is very complex. At the present time, most of the studies made have been unilateral, with little attempt to correlate specifically the actual flora of the abscess with the actual clinical progress. The status of the bacteriologic questions will be clarified by a specific consideration of some of the leading organisms.

The organisms most frequently discussed are Plaut-Vincent's organisms, the fusiform bacillus and the associated spirochetes. Smith,[3] whose work has been considerable, adds to these as usually present vibrio forms and cocci. Varney [7] makes quite a bit of the black pigment-producing anaerobe which, when sought, is frequently encountered. Ermatinger,[9] in 1928, segregated the cases studied into those of pulmonary abscess, bronchiectatic abscess and bronchiectasis. Hemolytic stapylococci were most commonly found, organisms of the genus Neisseria next, and commonly hemolytic streptococci. Pneumococci, Friedländer's bacillus, diphtheroid types, Proteus and others were noted. Cohen [8]

9. Ermatinger, L. H.: Microorganisms of Lung Abscess and Bronchiectasis, J. Infect. Dis. **43**:391 (Nov.) 1928.

called attention to a group of anaerobes described in connection with pulmonary gangrene in 1898, Bacillus ramosus, Bacillus furcosus, Bacillus thetoides and others which, as he correctly stated, have been ignored in the literature for some years. It is obvious from these and other studies that there may be found in specimens from pulmonary abscess rods, cocci and spirochetes, both aerobic and anaerobic. To list all the organisms that have been found would be beside the purpose, and it would be an injustice to those organisms that have not been identified. Importance is, for example, attached to members of the genus Leptothrix by some. A case recently encountered in San Francisco yielded a number of Pseudomonas pyocyanea, very likely of significance in the case, but rarely noted in other cases.

Considerable care is needed in the interpretation of bacteriologic results in connection with the specimen examined. Specimens come from sputum, from bronchoscopy, from lobectomy, from drainage, and so on. Since the flora of the abscess is to some extent duplicated in the flora of the buccal cavity, the specimen of sputum is at least confusing. A tabulation of the cases studied locally reveals that sputums examined yielded consistently greater numbers of organisms which may or may not have been present in the abscess. The pneumococcus, for example, based on comparison of the type of specimen examined, would seem to come from the buccal cavity in many of the cases in which it is found.

Passing on to the present status and the possible rôle of specific organisms, the fusiform bacillus and the spirochetes are frequently mentioned.

The status of the fusiform bacillus is somewhat as follows: Knorr,[10] Krumwiede and Pratt,[11] Tunnicliff [12] and many others have cultivated fusiform bacilli. Those who have studied these organisms as such agree that there are three or more types. However, the types are usually noted on simple morphologic grounds, a basis of differentiation that is notoriously unsatisfactory. Those who have made intimate morphologic studies go so far as to claim that giant cocci or spirilla may arise from fusiform rods.[13] One does not have to accept or to deny these radical conceptions to acknowledge the paucity of information regarding the organisms, or the necessity for having a reasonably firm background before attempting correlation with the pulmonary abscess. From the standpoint of comparative pathology, one may say that the organisms are often encountered in the mouth, ordinarily associated with gangre-

10. Knorr, M.: Centralbl. f. Bakt. (Abt. 1) **87**:536, 1921-1922; **89**:4, 1922-1923.

11. Krumwiede, C., and Pratt, J.: J. Infect. Dis. **12**:199, 1913; **13**:438, 1913.

12. Tunnicliff, R.: J. Infect. Dis. **3**:148, 1906.

13. Mellon, R. R.: J. Bact. **4**:505, 1919; New York State J. Med. **20**:187, 1920.

nous processes. Material containing the organisms, in association with spirochetes and unknown organisms, produces localized abscesses in the groins of guinea-pigs, and has induced pulmonary abscess. This knowledge is, however, unproved as to its specific relationships, and it seems likely that Cruikshank and Cruikshank [14] are correct in saying: "It is more probable that B. fusiformis is a secondary invader of tissues already diseased or devitalized. There seems little doubt that the organism helps to maintain or further the progress of ulcerative and gangrenous conditions."

The situation with regard to spirochetes also needs clarification. These organisms should not be confused with spirilla, but the literature is difficult to interpret on any basis other than that of confused terms. Spirochetes are wavy filaments, with varying numbers of curves and varying helicine morphology, motile and varying in size in defined species. The type that is most often associated with fusiform bacilli, Treponema vincenti, may or may not be identical with Treponema buccale. Few investigators are qualified to make the finer morphologic differentiations of the four or five types of oral spirochetes, if indeed such differentiation is adequate. Noguchi was well aware of the frequent association of spirochetes in pulmonary infection, and he was well qualified to differentiate types of spirochetes, yet his final publication treats the subject as being "a very complex one because of the simultaneous presence of all of these organisms." [15] We have thus expert opinion to the effect that there are various types of fusiform bacilli and various types of spirochetes, and to pool them for purposes of simplicity is most certainly unscientific. Granting that slow scientific results must, for the moment, be passed if a clinical advantage may otherwise be gained, it must still be shown, in those cases in which these organisms are found, either fusiform bacilli or spirochetes or both, that the organisms as a group are all invasive in gangrenous processes. Much more might be said about the spirochetes, and their relationship to fusiform bacilli, but let us consider another type of organism.

Diphtheroids are very frequently encountered in specimens from pulmonary abscess. To the uninitiated, this might seem significant. Diphtheroids, however, have no bacteriologic status whatever, and certainly no clinical status. They are usually differentiated morphologically, and the criteria differ, depending on the examiner. If one is to believe the present concepts of pleomorphism of bacteria, diphtheroids have been produced from tubercle bacilli, and they have been produced from

14. Cruikshank and Cruikshank, in Bensted, H. J., and others: A System of Bacteriology in Relation to Medicine, London, His Majesty's Stationery Office, 1929, vol. 8.

15. Noguchi, H., in Jordan, E. O., and Falk, I. S.: Newer Knowledge of Bacteriology and Immunology, Chicago, University of Chicago Press, 1928.

streptococci. In the light of present knowledge, it is as logical to suppose, perhaps, that the diphtheroids of the abscess are variants from other organisms as that they constitute a specific group with specific properties. And, if the latter more conservative view is held, what are those properties?

No significance is usually attached to organisms of the genus Neisseria, those gram-negative diplococci common to the nose and throat and frequently noted in pulmonary abscess. These organisms have specific characteristics, and may be cultivated, and the probability is that the environment of the abscess is favorable to their existence as commensals.

All types of streptococci have, at some time or other, been noted in pulmonary abscesses, speaking in general terms. The order of frequency is not certain, but the nonhemolytic type seems to head the list. That streptococci growing anaerobically are encountered is stated in various reports, and they were noted in local specimens. The evidence that these organisms are purely anaerobic is not convincing. Furthermore, the literature concerning them makes it impossible to state that there is a group of anaerobic streptococci which are purely anaerobic and which, hence, might be endowed with special capabilities in the production of necrotic processes.

One might expect the most significant organisms to be of the anaerobic types. In this field, only one of the Clostridium group, Cl. cochlearium, has apparently been recorded.[8] None of this group was found in local specimens, and Cohen found this one but once. Thus one may apparenty rule out for the most part those anaerobes encountered in gas gangrene and similar infections. The black pigment-producing organism is relatively new, and its pathogenic rôle is uncertain. The work of Goldman, in connection with local cases, confirms the reports, first, that the organism is common in specimens from pulmonary abscess, and second that it is difficult to isolate, although cultivation is relatively simple. This makes clear the reasons for the slow progress in assigning a definite rôle to the organism in the pathogenesis of infection, for, if active at all, it presumably requires association with other organisms, notably cocci. The anaerobes noted by Cohen, apparently not considered to date by anyone else, were not found regularly by him. It is quite possible that one or more of them might be present in a significant number of cases, and that this occurrence might have clinical weight. Pulmonary abscess is, in a sense, localized gangrene. It is accompanied by those signs which one associates with anaerobic organisms. That these organisms, vastly different in any characteristic that one might name except oxygen requirements, may be particularly important is claimed by some; but there seems to be little thus far to substantiate the hypothesis that this broad generalization necessarily obtains in pulmonary abscess, at least.

These brief sketches leave many stones unturned. Gram-negative rods, sometimes identified as B. coli or P. vulgaris, are not uncommon in specimens studied. King and Morgan,[16] two years ago, described a case in which Proteus was apparently responsible for multiple pulmonary abscesses. Pfeiffer's bacillus and Friedländer's bacillus,[17] and others encountered occasionally, are organisms known to have pathogenic significance under proper circumstances. The filamentous organisms, bordering on Actinomyces in type, constitute a group concerning which little is known fundamentally. Definite fungi and even amebas [18] no doubt account for rare abscesses, but it seems probable that these cases would have recognized features.

The demonstration of the clinical development of a case as correlated with the bacteriology is not yet possible. One author [19] stated that a more acute disease might possibly be expected in the presence of considerable numbers of streptococci. An analysis of the cases studied in San Francisco to date indicates that, in several cases, marked clinical differences may be associated with bacteriologic differences. What these differences are only further study will tell. Whether they will correlate with clinical development is also still an open question.

To define the possible approaches to a study of this nature would take as long as a comprehensive discussion of all the organisms involved, and not because the story would be the same. All sorts of schemes have been suggested—skin tests, phagocytic tests, serologic examination, blood cultures, innumerable experimental tests, and so on. No one knows what might be revealed, but in such a problem it is essential that one stand squarely. Many studies reveal a tendency to attempt to jump a fearful number of hurdles in the chance that one might, after all, cross the tape unscathed at the other end. The answer to so complicated an infection as pulmonary abscess is probably twenty years off rather than two, at least so far as the bacteriology is concerned.

By way of a summary, hope is expressed that two points may at least stand out. It is hoped that pulmonary abscess may be bacteriologically pictured as originating from an uncertain agent but ending in the clinical picture that includes a terrific secondary invasion of numbers of organisms of various and numerous types. And it is further hoped that surgeons may gain some slight insight into the bacteriologic questions per se that are involved. These questions are related directly to the clinical questions, could a reciprocal point of view but be obtained. It may perhaps be granted that an excellent clinician may have lost touch

16. King, M. J., and Morgan, R. H.: Am. Rev. Tuberc. **19**:182, 1929.
17. Graham, E. A.: S. Clin. North America **2**:1501, 1922.
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with much in bacteriology, and it will probably be readily granted that the bacteriologist finds it difficult to get a clinical point of view. Be that as it may, the problem is objective, not subjective; it involves both good clinical work and good bacteriology.

The authors are indebted to the clinical and bacteriologic members of the local group engaged in this problem. The entire group owes a great deal to Dr. Selling Brill, whose activity and enthusiasm was responsible for the organization of the study, and whose untimely death, in January, 1932, is a loss to the group and to the surgical profession.

GASTRIC SECRETION

III. INCREASED ACID SECRETION IN A TRANSPLANTED GASTRIC POUCH DURING LACTATION

EUGENE KLEIN, M.D.
NEW YORK

In four dogs with transplanted gastric pouches unusual phenomena were observed during lactation. The preparation and character of these pouches have been described in detail in two previous papers.[1] In brief, the operation was done in two stages. In the first, a portion of the body along the greater curvature was cut away from the stomach and then sutured to form a pouch. This pouch was transplanted to a space in the subcutaneous tissues. The gastric blood supply to the pouch was left intact. At a second operation from three weeks to several months later, these vessels were severed, leaving the pouch dependent on a new blood supply from the abdominal wall. A second type of pouch consisted only of mucous membrane and submucosa, the muscular coats, including the plexus of Auerbach, having been removed. The secretion of these pouches has already been reported in the papers mentioned.[1]

In the four dogs described in this paper, the first two had pouches of the first type. In the third, a pouch of the first type was prepared, but the second stage had not been performed when the dog gave birth to puppies. The gastric blood supply was therefore intact during lactation. In the fourth dog, a pouch of the second type was prepared.

In the first dog, L., the pouch was prepared on April 9, 1928, and tests for secretion showed results similar to those already reported. The second stage of the operation, that is, the severing of the gastric blood vessels, had not yet been performed when, five weeks after the first stage, I left on my vacation. On my return, I found that the pouch had turned itself inside out through its opening, and that there was on the abdominal wall a protruding mass covered with mucous membrane. At an operation three months after the first procedure, the mass was reinverted and the pouch reestablished. It was placed in a space in the subcutaneous tissues. A small opening was left to form a fistula for

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From the Surgical Service of Dr. A. A. Berg and from the Laboratory of the Mount Sinai Hospital.

1. (*a*) Klein, E., and Arnheim, E.: Gastric Secretion: I. A Transplanted Subcutaneous Gastric Pouch, Arch. Surg. **25**:433 (Sept.) 1932. (*b*) Klein, E.: Gastric Secretion: II. Studies in a Transplanted Gastric Pouch Without Auerbach's Plexus, ibid. **25**:442 (Sept.) 1932.

the collection of gastric juice. This fistula closed spontaneously, and very little secretion could be obtained from the pouch. It would slowly fill up and form a mass under the skin the size of a small egg. On puncture about every three weeks, a thick mucus with no acid was obtained. The dog then became pregnant. No change was noted during pregnancy. Four months after the second operation, six puppies were born. Three days later the pouch opened spontaneously, and a small erosion of the skin formed at the mouth of the fistula. One week after the puppies were born, free acid could be demonstrated following the feeding of meat (table 1). The erosion and the fistula gradually increased in size and reached their maximum from four to five weeks after parturition, when the erosion was about 4 by 5 cm. in area and from 1.5 to 2 cm. deep. A test (table 1) made at this time (Dec. 18,

TABLE 1.—*Dog L., with Transplanted Subcutaneous Gastric Pouch. Fed 200 Gm. of Meat at the Beginning of the First Hour* *

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Acid
11/30/28—One Week After Parturition			
1	0.1	..	..
2	0.6	50	83
3	1.0	25	50
4	0.8	10	33
12/18/28—During Lactation, About Four Weeks After Parturition			
1	2.2	88	105
2	1.3	85	100
3	1.4	82	93
4	1.1	77	86

* Gastric juice collected each hour from the fistula. In this and in all the succeeding tests free and total acid were determined by titration against tenth-normal sodium hydroxide with Toepfer's reagent and with phenolphthalein.

1928) with 200 Gm. of meat showed that the quantity of secretion had increased and that the free acid was markedly increased. The quantities of secretion varied in the succeeding tests, but remained around this level for about four weeks (about two months after parturition) and then diminished, although the free acid did not again disappear. The erosion progressively diminished in size, and three months after the puppies were born it was healed. The fistula, however, remained open.

The striking points observed were:

1. The reappearance during lactation of free acid secretion in a pouch that had been secreting only small quantities of mucus during pregnancy and before that time.

2. The digestion of the skin and subcutaneous tissues over a very wide area, even though the secretion was small in quantity.

3. The healing of the erosion at the end of lactation.

4. The drop in the quantity and acidity of the secretion after the end of lactation, although the sac did not revert to its old state. Secretion of free acid persisted.

In a second dog, F., in which a similar subcutaneous gastric pouch had been prepared (Jan. 8, 1929), the secretion had markedly diminished after the second stage of the operation, which consisted in severing the gastric blood vessels. It was then noted that the dog was pregnant. During the pregnancy there was no apparent increase in the secretion, as is shown in table 2 (March 19), taken nine days before the birth of seven puppies.

During pregnancy there had been no erosion around the mouth of the fistula. During lactation erosion began to take place, so that four weeks later there was extensive digestion of the skin and subcutaneous tissues over an area 5 by 7 cm. The results of a test for secretion done

TABLE 2.—*Dog F., with Transplanted Subcutaneous Gastric Pouch. Fed 200 Gm. of Meat at the Beginning of the First Hour*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Acid
3/19/29—Nine Days Before Birth of Puppies			
1	0.2	0	..
2	0.2	0	..
3	0.2	Trace	..
4	0.4	25	50
4/25/29—During Lactation, About Four Weeks After Parturition			
1	1.0	30	70
2	1.5	53	86
3	1.0	70	100
4	0.7	57	85

at this time are shown in table 2 (April 25). This table shows a fairly marked increase in the secretion and a decided increase in the free acid and total acid. The secretion gradually subsided, so that two months later it was down to the level it had been before lactation and the erosion had healed. The same phenomena were repeated in two subsequent pregnancies and lactations.

The third dog, N., was operated on April 16, 1929. A gastric pouch containing all the coats was transplanted into the subcutaneous tissues of the abdominal wall. On May 13, a test for secretion showed the results presented in table 3. At this time the original gastric vessels to the pouch had not yet been severed. On May 25, five puppies were born. A test on June 5 gave the results presented in table 3. The amount of the secretion and the acidity are markedly increased. The erosion around the opening of the fistula became very pronounced, just as in the first two dogs. On August 14, a little over two and one-half months after the puppies were born, the secretion had dropped to the

figures shown in table 3, and the erosion was practically healed. The important point to remember in this dog is that the gastric blood supply had not been severed at the time of lactation.

In the fourth dog, B., on Oct. 10, 1930, a transplanted pouch was prepared from mucous membrane and submucosa. This pouch was also made from the body of the stomach, but the wall of the pouch consisted of the mucous membrane and submucosa only. It was the first time an attempt was made to prepare this kind of a pouch, and perhaps the technic was not as good as that later developed. At any rate, the pouch gave very little secretion. The secretion consisted chiefly of mucus, but free hydrochloric acid could be demonstrated in it by Congo paper. The quantities were so small that adequate tests could not be performed.

TABLE 3.—*Dog N., with Transplanted Subcutaneous Gastric Pouch. Fed 200 Gm. of Meat at the Beginning of the First Hour. Gastric Vessels to This Pouch Intact*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Acid
5/13/29—Twelve Days Before the Birth of Puppies			
1	2.3	65	104
2	3.9	87	135
3	3.6	96	115
4	4.3	113	132
6/5/29—During Lactation, Eleven Days After Parturition			
1	4.5	104	122
2	8.0	118	136
3	9.7	130	144
4	8.5	146	158
8/14/29—About Two and One-Half Months After Parturition			
1	0.2	..	...
2	1.4	86	102
3	2.8	72	94
4	4.6	80	86
5	3.5	88	104

On December 26, four puppies were born. The puppies died soon after birth, so that there was no period of lactation. The quantities of secretion in the pouch did not increase, nor did any erosion appear around the fistula. On Jan. 9, 1931, the vessels to the pouch were cut, leaving it dependent on the abdominal wall for blood supply. The pouch secreted only a little mucus, and the opening was frequently dilated, but it often closed in spite of this. On June 6, during a state of pregnancy, the pouch was incised (the opening had closed) and found to contain mucus with free hydrochloric acid (35 cc. of tenth-normal solution). On June 23, a test for secretion was performed (table 4). This was the first time that enough secretion followed the ingestion of food to permit a consecutive test. Three days later five puppies were born. On July 5, the skin began to break down around the fistula. By July 15, the digested area was 4 by 6 cm. and extended through the skin and subcutaneous tissues. A test was done on July 2, one week after parturi-

tion (table 4). It showed a marked increase in secretion and an increase in concentration of the free and total acid. On August 13, the free acid had disappeared (table 4) and the quantity had diminished. The erosion was healed.

The important points are:

1. No increase of secretion during the first pregnancy and after it. There was no period of lactation owing to the death of the puppies.

2. Secretion in measurable amounts starting near the end of the second pregnancy. It had been present only in exceedingly small amounts before.

TABLE 4.—*Dog B., with Transplanted Subcutaneous Gastric Pouch Consisting of Mucous Membrane and Submucosa. Fed 200 Gm. of Meat at the End of the First Hour*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Acid	Total Chlorides
6/23/31—Three Days Before Birth of Puppies				
1. Fed 200 Gm. of meat	0.2	20	55	...
2.	0.7	35	85	144
3.	0.6	25	60	...
4.	0.4	15	60	148
5.	0.6	25	55	...
7/2/31—During Lactation, One Week After Parturition, Shows Marked Increase of Secretion				
1. Fed 200 Gm. of meat	0.7	0	30	...
2.	2.9	50	80	146
3.	2.4	60	90	144
4.	0.7	70	90	...
5.	1.9	60	85	148
6.	2.3	70	95	146
8/13/31—Six and One-Half Weeks After Birth of Puppies				
1. Fed 200 Gm. of meat	0	..	..	...
2.	0.45	0	45	...
3.	0.75	0	50	...
4.	0.60	0	60	...
5.	0.30	0	50	...
6.	0.25	0	55	...

3. A marked increase of secretion during the lactation following the second pregnancy, both in quantity and in concentration of free and total acid.

4. During lactation, the appearance, for the first time, of erosion of the skin and subcutaneous tissues around the mouth of the fistula.

5. After lactation, the disappearance of the response of free acid to food and the healing of the erosion.

COMMENT

The striking facts are: (1) the appearance of gastric secretion in transplanted pouches during lactation and (2) the marked erosion of the abdominal wall and the opening of the fistula.

The Appearance of Acid Secretion During Lactation.—In the first dog there was no secretion until lactation started. In the second and third dogs, secretion was present before and during pregnancy, but a marked increase of secretion took place only during lactation. In the second dog the same phenomena occurred during three periods of lactation. In the fourth dog secretion began near the very end of pregnancy and reached its maximum during lactation. In a previous pregnancy followed by death of the puppies there had been no lactation and no increase of secretion. In the fourth dog too the transplanted pouch consisted of mucous membrane and submucosa only.

Ivy and Farrell,[2] working with pouches similar to those of the first two dogs, reported that the secretion during pregnancy and lactation was increased 25 per cent. The results reported in the foregoing dogs differ from theirs in that the increased secretion occurred during lactation.

This increase of secretion may be explained in two ways. The first is the marked dilatation of the blood vessels in the abdominal wall accompanying lactation and the resultant increase of the blood supply.

It has previously been noted [1a] that following the second stage of the preparation of these pouches there is a drop in the quantity and acidity of the secretion. This stage consists, as stated, in section of the original gastric blood vessels, leaving the pouch dependent on the abdominal wall. The drop in secretion was thought most probably to be due to the sudden diminution in the blood supply. It is, of course, possible that in the foregoing dogs the opposite condition was present, and that the dilatation of the blood vessels of the abdominal wall and the increased blood supply permit the increased secretion. However, though this occurrence may be responsible in part, further consideration leads to the view that other factors are involved.

The literature does not give much information concerning the effect of blood supply on gastric secretion. Several years ago, Lim, Ivy and McCarthy [3] advanced a working hypothesis that gastric secretion was dependent on increased blood supply, but this was before they were convinced that a humoral stimulant existed for the secondary phase. Their results may be explained on the latter basis.

Some time ago, while seeking a simple method to produce anacidity, I experimented with a diminished blood supply to the body and fundus.

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2. Ivy, A. C., and Farrell, J. I.: Contributions to the Physiology of Gastric Secretion: VIII. Proof of Humoral Mechanism, New Procedure for Study of Gastric Physiology, Am. J. Physiol. **74**:639, 1925.

3. Lim, R. K. S.; Ivy, A. C., and McCarthy, I. E.: Contributions to the Physiology of Gastric Secretion by Local (Mechanical) and Chemical Stimulation, Quart. J. Exper. Physiol. **15**:13 and 55, 1925.

These experiments have not been reported. The idea was to diminish both the amount of blood which carried the necessary materials for the production of hydrochloric acid and, at the same time, the amount of the humoral stimulant responsible for the second phase of gastric secretion. The gastric artery, all the vasa brevia and the epiploica sinistra were tied. Thus the body and fundus could receive blood only through the branches anastomosing with the pyloric arteries and the epiploica dextra. No gangrene of the wall of the stomach ever followed this procedure. Evidently sufficient blood supply to prevent such a sequel reached the affected parts through collateral channels. In the tests, the gastric contents were aspirated every twenty minutes through a long no. 20 French catheter that was inserted into the stomach after feeding

TABLE 5.—*Gastric Secretion Before and After Ligation of the Gastric Artery, the Vasa Brevia and the Epiploica Sinistra* *

Time	Free Acid	Total Acid
Before Ligation of Vessels		
20 min.	0	25
40 min.	0	30
1 hr.	0	45
1 hr. 20 min.	10	55
1 hr. 40 min.	25	75
2 hr.	45	90
2 hr. 20 min.	40	90
After Ligation of Vessels		
20 min.	0	20
40 min.	0	25
1 hr.	0	35
1 hr. 20 min.	0	45
1 hr. 40 min.	25	70
2 hr.	35	80
2 hr. 20 min.	35	75

* Secretion was obtained by aspirating every twenty minutes through a catheter left in place (see text) following a meal of 200 Gm. of meat and 150 cc. of fresh salt-free broth.

the dogs 200 Gm. of meat and 150 cc. of salt-free fresh broth. The catheter was left in situ and brought out through a space between two teeth. A specially constructed muzzle prevented the dog from biting the catheter. After closure of the blood vessels mentioned, the concentration of the hydrochloric acid in the stomach was only moderately reduced (table 5). If, in addition, the left vagus was cut just below the diaphragm, there was a more marked change. Section of both vagi [4] and ligature of the vessels usually caused an anacidity (table 6), but free hydrochloric acid could occasionally be demonstrated. These tests gave information only as to the concentration of acid in the stomach, and not as to the actual quantity of the secretion. In all cases (even without section of the vagi) there was a tremendous dilatation of the

4. The purpose of sectioning the vagi was to eliminate the psychic phase in addition to the secondary phase, the elimination of which had been attempted by the vessel ligation.

body and fundus of the stomach to four or five times the normal size. There was also a marked stasis of food, so that dogs killed eight hours after a meal showed enormous stomachs full of food—much more than was taken at the last meal. It was therefore evident that the method was not feasible clinically for the lowering of acidity.

In summarizing the facts concerning the blood supply, it may be said that (1) it is possible that the increased secretion during lactation is due in part, at any rate, to the increased blood supply, but that (2) no definite experimental evidence has been found that increased circulation produces such an effect and that (3) markedly diminishing the blood supply of the whole stomach only moderately affects the secretion.

TABLE 6.—*Gastric Secretion Before and After Intra-Abdominal Section of Both Vagi at Level of Diaphragm and Ligation of the Gastric Artery, the Vasa Brevia and the Epiploica Sinistra* *

Time	Free Acid	Total Acid	Pepsin†	Total Chlorides†
Before Section of Vagi and Ligation of Vessels				
20 min.	0	25	...	...
40 min.	0	35	64	140
1 hr.	0	30	...	...
1 hr. 20 min.	0	35	...	...
1 hr. 40 min.	0	40	100	144
2 hr.	35	85	...	...
2 hr. 20 min.	50	110	...	...
2 hr. 40 min.	40	90	144	156
3 hr.	30	100	...	...
3 hr. 20 min.	50	110	288	158
After Section of Vagi and Ligation of Vessels				
20 min.	0	10	64	...
40 min.	0	10	...	142
1 hr.	0	20	...	...
1 hr. 20 min.	0	25	100	142
1 hr. 40 min.	0	20	...	...
2 hr.	0	20	256	140
2 hr. 20 min.	0	25	...	...
2 hr. 40 min.	0	20	228	148
3 hr.	0	25	...	...

* Secretion was obtained by aspirating every twenty minutes through a catheter left in place (see text) following a meal of 200 Gm. of meat and 150 cc. of fresh salt-free broth.

† Pepsin is expressed in Mett units. Total chlorides are expressed as cubic centimeters of tenth-normal solution.

Much experience with normal and pathologic gastric secretion has left the feeling that the so-called primary and secondary phases as they are known may not tell the whole story of the secretion. For instance, removal of even three fourths of the stomach, especially in intractable cases of ulcer, can still leave the patient with hyperacidity, although in the large majority of cases a hypo-acidity or an anacidity is produced. Some variation exists in the secreting mechanism of these persons. Any facts, therefore, suggesting leads as to further possible factors influencing secretion deserve careful consideration. For that reason due weight has been given the hypothesis that an increased blood supply

may be responsible for the foregoing phenomena. Yet this explanation does not seem to be entirely adequate, and one is justified in seeking an additional cause.

One would naturally turn next to the state of lactation itself. There are two sets of observations that prompt one to do this. In the first place, in the third dog the pouch was still supplied by its normal gastric vessels and was not dependent on the abdominal wall for its blood supply. It is unlikely that these gastric vessels supplied more blood during lactation. But, of course, it may still be argued that the blood vessels of the abdominal wall dilated and thus furnished additional blood. This seems less likely in view of the finding of Hollander,[5] who had a dog with a Pavlov pouch in which he noticed that the secretion increased only during lactation and not during pregnancy. Pavlov pouches are intra-abdominal, and the normal gastric blood and nerve supply are not disturbed. It is difficult to see how an increased blood supply could have operated in this case. One is further justified in concluding that the responsible factors for this increase of secretion act through the blood stream, as the transplanted pouch in the fourth dog consisted only of mucous membrane and submucosa. All the gastric blood supply, the vagus, the sympathetics and the intrinsic myenteric plexus had been eliminated. Only blood vessels of the peripheral abdominal wall supplied it.

Though one is apparently justified, then, in seeking an additional cause, in the present state of knowledge it is hard to say what factors associated with lactation may be responsible for the increase of gastric secretion. One naturally turns to the cause of lactation. Corner[6] has recently contributed evidence to show that this is due to a secretion from the anterior pituitary gland. No facts are as yet available to show whether the latter influences gastric secretion. The work of Cushing[7] showing the stimulating effects of posterior pituitary extract on the vagus system should also be mentioned. Whether during lactation an increase of the posterior pituitary secretion accompanies the increased anterior pituitary secretion has also not been investigated. Both these problems deserve careful study. But regardless of whether the pituitary or some other cause is responsible, it seems quite definite that some condition accompanying lactation has increased the secretion in these dogs, and when it is realized that this secretion is accompanied by the marked erosion to be presently discussed, it assumes greater significance.

5. Hollander, F.: Gastric Hypersecretion Following Parturition in a Dog, Proc. Soc. Exper. Biol. & Med. **27**:303, 1930.

6. Corner, G. W.: Hormonal Control of Lactation, Am. J. Physiol. **95**:43, 1930.

7. Cushing, H.: I. The Reaction to Posterior Pituitary Extract (Pituitrin) When Introduced into the Cerebral Ventricles, Proc. Nat. Acad. Sc. **17**:163, 1931.

The Marked Erosion of the Fistula and the Abdominal Wall.—The second striking point noted about the pouches was the marked erosion of the abdominal wall that occurred around the fistula during lactation. The secretion, as shown in the tests, was certainly not profuse, but the erosion was more extensive than is usually seen in actively secreting Pavlov pouches in which the response to a meal is from 5 to 8 cc. per hour. In these pouches it was from 0.3 to 1 cc. per hour. The two possible explanations that present themselves are that (1) the juice, though small in quantity, was of a greater digestive power than normal and (2) the tissues of the abdominal wall were less resistant to the digestive factors in the juice.

Unfortunately the quantities of the secretion were so small that adequate determinations of pepsin could not be made. But in the tests that were performed by the Mett method in the third dog, there did not appear to be an excessive amount of pepsin.

The second possibility, as before mentioned, is that there is a diminished resistance to the digestive juice. A consideration of this question involves, of course, a discussion of the resistance of living cells to ferments. A very extensive literature exists on this subject,[8] and it chiefly revolves about the question of antiferment. Whether or not in the foregoing experiments there existed a diminution of antiferments in the tissues of the abdominal wall cannot be stated at present.

However, whichever of these two factors may be the significant one, it seems quite definite that an imbalance existed, and the potency of a small amount of gastric juice in creating the severe digestive erosions was very striking. It may incidentally be recalled what marked variations exist in persons in the amount of erosion present around a gastric fistula.

The rôle of gastritis as a precursor of ulcer has recently been widely discussed (Konjetzny). Some observers think that acid and pepsin are important elements in the production of gastritis. In patients in whom it develops, some such imbalance may be responsible.

The observation, then, that increased secretion takes place in transplanted gastric pouches during lactation and that the resultant juice possesses a greater than normal digestive power toward the tissues of the abdominal wall of the same animal may be of clinical importance. Further lines of investigation of the subject are readily suggested, as indicated.

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8. Some of the more important recent articles are: Dragstedt, L. R., and Vaughn, A. M.: Gastric Ulcer Studies, Arch. Surg. **8**:791 (May) 1924. Necheles, H.; Ling, J., and Fernando, F.: The Fate of Organs Transplanted into the Duodenum, Am. J. Physiol. **79**:1, 1926. Necheles, H., and Fernando, F.: The Rôle of Trypsin and Anti-Trypsin, Am. J. Physiol. **79**:9, 1925. de Takáts, G., and Mann, F. C.: The Effect on the Jejunal Mucosa of Transplantation to the Lesser Curvature of the Stomach, Ann. Surg. **85**:698, 1927.

SUMMARY AND CONCLUSIONS

1. In gastric pouches transplanted to the subcutaneous tissues of the abdominal wall and completely separated from the old blood and nerve supply there was an increase of the quantity of secretion and of the concentration of hydrochloric acid during lactation. This was repeatedly observed.

2. When no secretion was present prior to lactation, it first appeared during that time.

3. In one case in which all the puppies died and there was no period of lactation, no increased secretion was observed.

4. Accompanying this increased secretion was a marked erosion of the abdominal wall around the opening of the pouch that was entirely out of proportion to the quantity of the secretion.

5. The possibility is discussed that the dilatation of the blood vessels in the abdominal wall during lactation is responsible for these phenomena by increasing the circulation. After a consideration of the factors, including experiments on diminishing the blood supply, the conclusion is reached that though a vascular supply may in part be responsible, other factors also play a rôle.

6. That these other factors are associated with the state of lactation itself is rendered probable, as the same phenomena were also observed when the original gastric blood supply was intact and when the blood supply of the abdominal wall was not concerned.

7. The causative factor for the increased secretion is at least partly humoral, since in one dog the transplanted pouch consisted only of mucous membrane and submucosa completely severed from the stomach. The vagus, the sympathetics, the gastric blood vessels and the myenteric plexus were eliminated.

GASTRIC SECRETION

IV. THE EFFECT OF ATROPINE ON THE SECRETION OF TRANSPLANTED GASTRIC POUCHES

EUGENE KLEIN, M.D.
NEW YORK

A perusal of the results obtained by the clinical and experimental use of atropine on gastric secretion is bewildering. In part, this is due to the facts that (1) different sorts of stimuli are used to induce secretion (various kinds of test meals, alcohol, histamine) and that these stimuli vary not only in quality but in quantity, (2) that the amounts of atropine used to inhibit the secretion vary and (3) that the atropine is administered in different ways, for instance, by mouth or subcutaneously. Nevertheless, the impression is gained that the foregoing variables alone do not account for the diversity of results.

The commonly accepted classification of gastric secretion is: (1) the primary or cephalic, (2) the secondary or gastric and (3) the intestinal.

The primary phase is reflex, and the impulse is transmitted to the stomach over the vagi following the seeing, smelling, tasting or chewing of food. Since atropine depresses the parasympathetic system, one would expect it to depress or inhibit completely this primary phase. That this is true in dogs was demonstrated by Uschakow.[1]

What atropine does to the secondary or gastric phase of secretion is, however, not so clear. This phase follows the entrance of food into the stomach and is due to chemical stimulation acting on the antrum or the distal portion of the stomach. Either the chemical stimuli (secretogogues) are directly absorbed into the blood stream through the antrum, or a hormone is formed in the antrum and carried to the glands of the body and fundus.[2] The latter view is the more prevalent. The vagi also seem to be concerned in the mechanism of this phase (Orbeli [3]), for after their section the secretion is diminished.

From the Surgical Service of Dr. A. A. Berg and from the Laboratory of the Mount Sinai Hospital.

1. Uschakow: Diss., St. Petersburg, p. 20; quoted by Babkin, B. P.: Die äussere Sekretion der Verdauungsdrüsen, Berlin, Julius Springer, 1928, p. 398.

2. For a summary of the subject, see Ivy, A. C.: The Rôle of Hormones in Digestion, Physiol. Rev. **10**:282, 1930.

3. Orbeli, L. A.: De l'activité de glandes à pepsine avant et après la section des nerfs pneumogastriques, Arch. di sc. biol. **12**:71, 1906.

The third phase is the intestinal. It, too, is due to chemical stimuli, either directly absorbed into the blood stream or first causing a hormone to be formed. This phase is inhibited by atropine (Ivy, Lim and McCarthy [4]).

The experiments to be reported here are chiefly concerned with the effect of atropine on the secondary or chemical phase. As some of the studies were on dogs with Pavlov pouches, however, observations on the primary phases are also included.

METHODS

Three types of dogs were used:

1. Two dogs with the usual Pavlov pouches (fig. 1). These pouches are supplied by both vagus and sympathetic nerves and by the normal blood supply. They are supposed to mirror accurately the secretory conditions in the whole stomach.

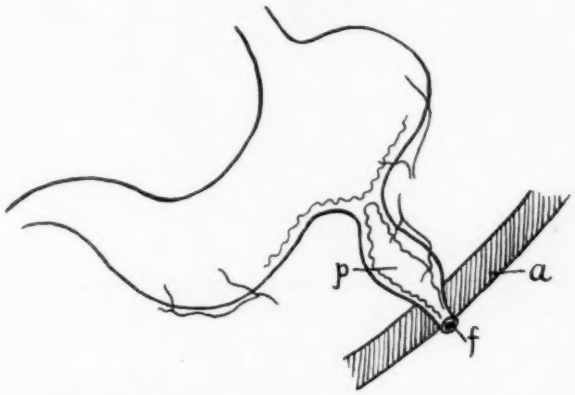

Fig. 1.—Pavlov pouch. Blood vessels and nerves intact. Only mucous membrane divides pouch lumen from stomach. The pouch is indicated by *p;* the abdominal wall by *a,* and fistula of pouch by *f.*

2. A dog with a Haidenhain pouch (fig. 2). This type of pouch is entirely separated from the stomach and is believed to have no vagus innervation. It is possible that sympathetic nerves still reach it along the blood vessels.

3. Four dogs with transplanted subcutaneous gastric pouches (fig. 3) prepared only from the mucous membrane and submucosa of the body and fundus (Klein [5]). In these pouches the vagi, the sympathetics and the myenteric (Auerbach's) plexus are eliminated. They are dependent for their blood supply on the abdominal wall and have no other communication with the gastric blood supply. In one of the dogs of this group, however, the original blood supply was left intact.

4. Ivy, A. C.; Lim, R. K. S., and McCarthy, J. B.: The Intestinal Phase of Gastric Secretion, Quart. J. Exper. Physiol. **15**:55, 1925.

5. Klein, E.: Gastric Secretion: II. A Transplanted Subcutaneous Gastric Pouch Without Auerbach's Plexus, Arch. Surg. **25**:442 (Sept.) 1932.

In the first type of dog both primary or vagal and secondary or humoral phases of secretion were present. In the third type, only humoral secretory stimuli reached the pouch, and atropine was therefore necessarily limited in its effect on stimuli carried through the blood stream. The possible sites for its action were further narrowed by the removal of the myenteric plexus.

In the majority of tests 1 mg. of atropine was injected subcutaneously. This dose was used because it gave definite evidences of physiologic effect and was never toxic. Keeton, Luckhardt and Koch [6] had reported that they could con-

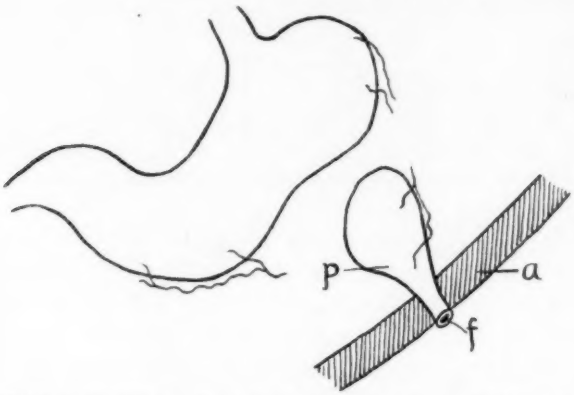

Fig. 2.—Haidenhain pouch. Vagi severed. Some sympathetic nerves enter with blood vessels, which are left intact.

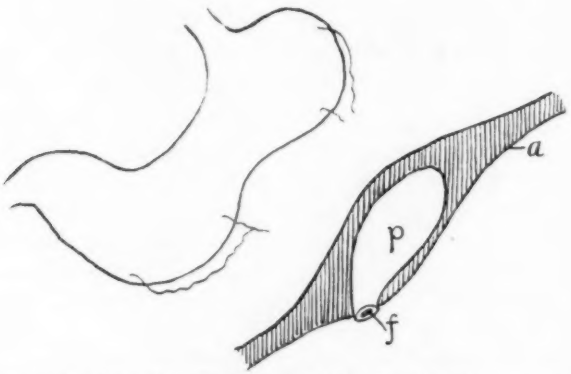

Fig. 3.—Transplanted subcutaneous pouch. Gastric blood vessels, vagi and sympathetic nerves completely severed. Myenteric plexus removed. Pouch walls consist of mucous membrane and submucosa.

stantly produce an anacidity in dogs with the same dose. They used it intramuscularly. The dogs all weighed from 10 to 12 Kg. The injection was usually given after an hour of control observation and was then followed fifteen minutes later

6. Keeton, R. W.; Luckhardt, A. B., and Koch, F. C.: Gastrin Studies: Response of the Stomach Mucosa to Food and Gastrin Bodies as Influenced by Atrophine, Am. J. Physiol. **51**:469, 1920.

by a meal of 250 Gm. of meat and 250 cc. of water. Occasionally the atropine was given at the time of the meal or earlier. Secretion was collected from the pouches every hour. Free acid was tested by Toepfer solution against tenth-normal sodium hydroxide and total acid by phenolphthalein. When sufficient secretion was present, determinations of pepsin and total chloride were often made. Pepsin was determined by Mett tubes after diluting the secretion sixteen times with twentieth-normal hydrochloric acid and incubating for twenty-four hours. The results are expressed as units of pepsin determined by squaring the millimeters of pepsin

TABLE 1.—*Action of Atropine on Pavlov, Haidenhain and Transplanted Gastric Pouches Without a Myenteric Plexus. One Milligram Was Injected Subcutaneously Fifteen Minutes Before a Meal of 250 Gm. of Meat and 250 Cc. of Water. Control Tests Are Made Without Atropine*

Hour	Volume of Juice, Cc.		Free Hydrochloric Acid		Total Hydrochloric Acid	
	Without Atropine	After Atropine	Without Atropine	After Atropine	Without Atropine	After Atropine
Dog M., with Pavlov Pouch						
1	0.6	0.9	56	26	92	40
Fed meat and water						
2	11.0	0.2	78	0	120	0
3	13.5	0	38	—	82	—
4	10.2	0	40	—	86	—
5	9.0	0.4	36	18	74	30
6	7.2	0.8	46	16	96	36
Dog N., with Haidenhain Pouch, 1.5 Mg. Atropine Used						
Fed meat and water						
1	1.2	0.2	78	0	96	+
2	1.4	0.5	86	0	102	6
3	2.8	0.7	72	0	94	8
4	4.6	1.2	80	Trace	86	6
5	3.5	2.0	88	8	104	10
Dog A., with Transplanted Gastric Pouch without Myenteric Plexus						
1	...	1.8	..	0	..	35
Fed meat and water						
2	2.2	2.7	55	0	75	35
3	3.5	2.8	70	0	95	30
4	3.8	1.6	75	0	100	35
5	5.5	1.4	70	0	95	40
6	2.5	0.6	85	0	110	30
Dog C., with Transplanted Gastric Pouch without Myenteric Plexus						
1	0.1	0	—	—	—	—
Fed meat and water						
2	1.3	0	75	—	120	—
3	0.8	0	60	—	115	—
4	1.2	0	50	—	100	—
5	0.9	0	55	—	115	—
6	0.6	0	70	—	125	—

digested and multiplying by sixteen. The total chlorides are expressed as cubic centimeters of tenth-normal solution to make them easily comparable with the free and total acid.

RESULTS

1. Atropine in doses of from 1 to 1.5 mg. given in the manner outlined can suppress the secretion of free hydrochloric acid in Pavlov, Haidenhain and transplanted subcutaneous gastric pouches (table 1). This indicates that in these tests atropine abolished the secretion. It is interesting to note that the second or Haidenhain pouch was the only one that never became anacid after the administration of 1 mg. of atropine;

1.5 mg. was necessary. Whether this was due to an imbalance created by the absence of the vagi and presence of sympathetics can only be conjectured.

2. In the dog with the latter type of pouch, 1.5 mg. of atropine given five minutes after a meal produced merely a decreased secretion. When

TABLE 2.—*Action of Atropine on Dog N., with Haidenhain Pouch Before and After Meal of 250 Gm. of Meat and 250 Cc. of Water*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Hydrochloric Acid
1.5 Mg. Atropine Injected Five Minutes after Meal			
1	1.7	10	14
2	2.6	12	14
3	3.5	12	14
4	2.3	10	12
5	2.0	8	10
1.5 Mg. Atropine Injected Five Minutes before Meal			
1	0	—	—
2	0	—	—
3	0.2	0	+
4	0.2	0	+
5	0.8	0	10

TABLE 3.—*Effect of Injecting 1 Mg. of Atropine Fifteen Minutes After 1 Cc. of Histamine, Showing That Atropine Does Not Abolish the Histamine Secretion*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Hydrochloric Acid
Dog A., with Transplanted Gastric Pouch without Myenteric Plexus			
1	0.2	0	45
1 mg. atropine injected subcutaneously 15 minutes after histamine			
2 hr. 15 min	2.7	40	70
3 hr. 15 min	0.4	0	45
4 hr. 15 min	0.65	0	35
5 hr. 15 min	0.8	0	35
6 hr. 15 min	0.5	0	25
Dog Cae., with Transplanted Gastric Pouch without Myenteric Plexus			
1	1 drop	0	—
1 Mg. atropine injected subcutaneously 15 minutes after histamine			
2 hr. 15 min	5.2	100	120
3 hr. 15 min	0.4	45	60
4 hr. 15 min	0	—	—
5 hr. 15 min	0	—	—
6 hr. 15 min	0	—	—

given thirty minutes before the meal, anacidity resulted (table 2). In the latter case, an atropinized animal to which the secretory stimulus was applied was being dealt with. In the former, the primary phase of secretion had already been stimulated, and perhaps some of the food in the stomach had initiated the secondary phase. Rall,[7] one of the few observers who reported anacidity after the administration of atropine

7. Rall, T.: Ueber den Einfluss des Atropins auf die sekretorische und motorische Funktion des gesunden Magens, Ztschr. f. d. ges. exper. Med. **52**:752, 1926.

TABLE 4.—*Effect of Injection of 1 Mg. of Atropine Fifteen Minutes Before Ingestion of 250 Gm. of Meat and 260 Cc. of Water, Showing That When Secretion of Hydrochloric Acid Was Present During the Control Hour Atropine Did Not Abolish Secretion, and When It Was Absent the Atropine Did Abolish the Secretion*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Hydrochloric Acid	Pepsin	Total Chlorides
Dog E., with Pavlov Pouch					
1	1.2	50	85	...	...
Fed meat and water fifteen minutes after atropine subcutaneously					
2	2.8	55	70	400	156
3	2.5	95	105	144	156
4	2.3	80	95	...	140
5	2.5	90	100	672	154
6	3.1	80	95	576	150
Experiment Repeated on Same Dog When No Secretion Was Present in the First Hour					
1	0.2	0	—	...	...
Fed meat and water fifteen minutes after atropine subcutaneously					
2	0.3	0	45	...	...
3	0.5	0	50	...	...
4	1.0	30	85	...	...
5	2.0	75	95	144	150
6	1.8	80	110	256	160
Dog Cae., with Transplanted Gastric Pouch without Myenteric Plexus					
1	4.9	45	80	16	148
Fed meat and water fifteen minutes after atropine subcutaneously					
2	3.1	50	70	16	144
3	9.6	40	75	9	142
4	1.0	25	60	...	...
5	1 drop	—	—	...	...
6	0	—	—	...	...
Experiment Repeated on Same Dog When No Secretion Was Present in the First Hour					
1	0	—	—	...	...
Fed meat and water fifteen minutes after atropine subcutaneously					
2	0	—	—	...	...
3	0	—	—	...	...
4	0.3	35	60	...	...
5	0.4	25	55	...	...
6	0.4	30	65	...	...

TABLE 5.—*Effect of Injection of 1 Mg. of Atropine on Spontaneous Secretion in Dog Cae., Having Transplanted Gastric Pouch Without Myenteric Plexus*

Hour	Volume of Juice, Cc.	Free Hydrochloric Acid	Total Hydrochloric Acid
1	1.4	110	120
1 mg. atropine injected subcutaneously			
2	1.6	72	80
3	0.6	30	60
4	2.7	50	70
5	1.1	30	52
6	0	—	—

in man, noticed the same fact. He used bouillon as a test meal. One milligram of atropine, one hour before the meal, produced anacidity. At the time of the meal it was ineffectual. The possible cause will be discussed later.

3. If 1 cc. of histamine was administered fifteen minutes after 1 mg. of atropine, the response to histamine was almost the same as without the atropine. Occasionally it was slightly reduced. This was true of all the types of pouches (table 3). It had previously been observed by Keeton, Luckhardt and Koch [6] in Pavlov pouches. It is evidently true of the Haidenhain pouch and of the transplanted pouch without the myenteric plexus.

4. Two dogs showed another interesting phenomenon. One of these was of the first group (with a Pavlov pouch) and one of the last group. In the latter a pouch, consisting only of mucous membrane and submucosa, had been transplanted as in the others, but the original blood supply was left intact. At times 1 mg. of atropine inhibited the secretion; at other times it did not. Examples are shown in table 4. Analysis of these results showed that when secretion was present during the control hour the atropine was ineffectual. When no secretion was present, the atropine inhibited the stimulus of food. This was repeatedly observed. In the dog with the transplanted pouch it was also found that spontaneous secretion such as noted in the control hour frequently occurred. This has previously been reported in this type of pouch (Klein [5]). Atropine lowered but did not abolish this spontaneous secretion (table 5). There is evident here a stimulus that is apparently humoral and which, like histamine and gastrin, is not completely suppressed by atropine.

COMMENT

In the foregoing experiments two observations should be emphasized: 1. Following a meal of meat and broth atropine can abolish the secretion of free hydrochloric acid in a Haidenhain pouch and in transplanted pouches. The latter were without vagus or splanchnic innervation and without the myenteric plexus. This would tend to show that in dogs atropine can abolish the humoral secretion of the secondary or gastric phase. Stimuli from the stomach could reach the latter pouches only through the blood stream.

2. In two dogs when secretion of free hydrochloric acid was present before the tests began the atropine was ineffectual. This was noted in a dog with a Pavlov pouch, but was especially marked in a dog with a transplanted pouch. In the case of the dog with a Pavlov pouch it is possible that the spontaneous secretion may have been vagal and similar to the fasting secretion in man. If so, it is likely that the atropine would have inhibited it. In the dog with the transplanted pouch, however, this

secretion was necessarily humoral and not reflex in nature. Like the secretion of histamine, it could not be abolished by atropine in doses of 1 mg.

The origin of this secretion is obscure, but it must have come either from the gastro-intestinal tract or from the parenteral tissues. As the dog had not been fed for twenty-four hours, stimulation by food from the stomach and small intestine seems excluded. Food substances introduced into the large intestine through the rectum do not stimulate gastric secretion. Saliva, bile and pancreatic juice in the stomach are known to stimulate the second phase. However, it would seem that since the other intragastric stimuli (water, meat) were rendered ineffectual by atropine, these also may have been inhibited. There is left the interesting possibility that the humoral stimulant was of parenteral origin. Such parenteral stimuli have previously been assumed by Bickel [8] and Krimberg.[9] In view of the fact that atropine did not abolish this stimulus, it probably acts like histamine directly on the cell.

On the other hand, atropine did completely inhibit the action of the humoral stimuli which originated from food inside the stomach, that is, from the test meal. This observation was previously made in a different way by Zeliony and Sawitsch [10] and by Sanozky.[11] The former found, for instance, that the secretion due to beef extract placed in an antral pouch could be inhibited by atropine. But if the beef extract were injected subcutaneously or intravenously, atropine could not prevent the secretion.

The question naturally arises as to why the atropine inhibits the humoral stimulus produced by food but does not inhibit the humoral secretion of parenteral origin. Two possible answers to this question are: 1. The secretory hormone produced by food in the antrum and intestine may differ chemically from the other humoral stimulant, and also from other substances, such as beef extract, histamine and gastrin, which, after subcutaneous injection, cause secretion; further, the latter may act directly on the secretory cell, while the hormone may act on nerve endings that are paralyzed by atropine, or (2) atropine prevents the formation of the gastric hormone in dogs. The first possibility cannot be answered until more is known of the hormone. The second possibility will be discussed.

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8. Bickel, A.: Der nervöse Mechanismus der Sekretion der Magendrüsen und der Muskelbewegung am Magendarmkanal, Ergebn. d. Physiol. **24**:228, 1925.

9. Krimberg, R.: Zur Frage nach der Bedeutung der Muskelhormone im Sekretionsprozesse der Verdauungsdrüsen, Biochem. Ztschr. **157**:187, 1925.

10. Zeliony and Sawitsch: Verhandl. d. ges. russ. Aerzte zu St. Petersburg, 1912; quoted by Babkin (footnote 1, p. 399).

11. Sanozky: Diss., St. Petersburg, 1893, p. 80; quoted by Babkin (footnote 1, p. 398).

The Site of Action of Atropine.—The site of action of atropine is usually considered to be on the postganglionic nerve endings in the cells or neurocellular substance, but the subject is not clearly settled. There is some evidence, for instance, that in large doses it may act directly on the gastric secretory cells (Keeton, Luckhardt and Koch [6]). In the case of the motor cells the chief action also seems to be on the nerve endings or neuromuscular junction. But here it has more definitely been shown (Cushny [12]) that atropine may also act directly on the cell.

The foregoing experiments definitely show that complete inhibition of secretion may be produced by atropine in the absence of the myenteric plexus. More precise conclusions as to the site of action could be drawn from these experiments if one were certain of the nature of the submucous (Meissner's) plexus. If the latter were definitely sympathetic, then the postganglionic vagus fibers to the secreting cells would originate in the myenteric plexus. Since this plexus had been removed and since the sympathetics were also eliminated, the secreting cells of the transplanted pouch would then be left without any efferent nerve endings. Both autonomic systems would be eliminated. But although there does exist evidence that the submucous plexus is sympathetic and although in a previous paper I subscribed to this view, I am at present uncertain as to this. The possibility therefore still exists that atropine could act on nerve endings in the pouches mentioned. This subject will be more fully discussed in a subsequent paper on the action of pilocarpine.

One other possible site of action deserves further mention. Ivy [2] advanced the suggestion that atropine may prevent the formation of the hormone in the stomach. There is no parallel action of such a nature known, but, as already stated, this hypothesis would explain the experiments of Zeliony and Sawitsch.[10] If beef extract was placed in the antrum of the stomach, atropine inhibited the secretion, but after subcutaneous injections atropine was ineffectual. This hypothesis would also explain the observation mentioned that the same dose of atropine which before a meal inhibited secretion was ineffectual if given after the onset of the meal. It is possible that when given before the meal it prevented the formation of hormones, and that after the latter had been formed and were already present in the blood the atropine was ineffectual.

In the dog, then, atropine can abolish all three phases of secretion. Uschakow [1] showed that it could abolish the first phase. Sanozky and Zeliony and Sawitsch showed that it abolished the secretion due to chemical stimuli in the stomach, and I have now shown the same result in transplanted pouches deprived of all peripheral nerve supply and

12. Cushny, A. R.: Handbuch der experimentellen Pharmakologie, translated into German by A. Heffter, Berlin, Julius Springer, 1920, vol. 2, pt. 2, p. 631.

subject only to humoral influences. Ivy, Lim and McCarthy [4] reported that it abolishes the intestinal phase.

Action of Atropine on Man.—In man, however, the reports on the action of atropine vary considerably. On the one extreme are results such as those of Crohn,[13] who found an increase, and on the other, results of Rall,[7] who found complete abolition. The majority of observers report only a reduction in acidity which varies in different groups of subjects (Keefer and Bloomfield,[14] Schiff,[15] Bennett,[16] Lockwood and Chamberlin,[17] Kellerman [18]).

It cannot be said conclusively that atropine always abolishes the primary or reflex phase in man, but there are some suggestive facts. Thus Winkelstein [19] reported that after partial gastrectomy and removal of the second phase atropine probably suppresses the primary or reflex phase.

The chemical phase cannot, however, be suppressed. Pokras and Michelson [20] attempted to produce a condition in which the primary phase was eliminated by feeding the patients through a stomach tube. In ten of fifteen cases the resultant secretion could be diminished in varying degrees. Kliutschareff [21] from similar studies came to the conclusion that in cases of gastric hyperacidity a definite drop with atropine can be obtained only if a large part of this hypersecretion is due to the first phase. Hypersecretion is, of course, not normal.

The reason for this difference of action in the second phase between man and dog is unknown. It is possible, however, that in man more of the humoral stimuli act directly on the cell. Under these conditions atropine would be relatively less effectual.

Hypersecretion is usually considered to be of nerve origin. Should a condition such as humoral hypersecretion be established, its origin and

13. Crohn, B. B.: Am. J. M. Sc. **155**:801, 1918.

14. Keefer, C. S., and Bloomfield, A. L.: The Effect of Atropine on Gastric Function in Man, Arch. Int. Med. **38**:303 (Sept.) 1926.

15. Schiff, Arthur: Beiträge zur Physiologie und Pathologie der Pepsinsecretion, Arch. f. Verdauungskr. **6**:107, 1900.

16. Bennett, T. I.: The Modification of Gastric Function by Means of Drugs, Brit. M. J. **1**:366 (March 3) 1923.

17. Lockwood, B. C., and Chamberlin, H. G.: The Effect of Atropin on Gastric Function, as Measured by Fractional Analysis, Arch. Int. Med. **30**:806 (Dec.) 1922.

18. Kellerman, Emil: Untersuchungen mit der fraktionierten Magenausheberung, Arch. f. Verdauungskr. **45**:67, 1925.

19. Winkelstein, Asher: Gastric Secretion After Partial Gastrectomy for Ulcer, Am. J. Surg. **7**:494, 1929.

20. Pokras, S., and Michelson, V.: Vegetatives Nervensystem und Magensekretion, Arch. f. Verdauungskr. **38**:373, 1926.

21. Kliutschareff, quoted by Pokras and Michelson (footnote 20).

nature would be of significance. For instance, the production of gastric anacidity after partial gastrectomy (which removes the antrum and therefore the chemical phase) would depend in part on the proportion of stimulating influences arising from the antrum. Perhaps in these relations lies a partial explanation of the observation mentioned in a previous paper;[22] namely, that partial gastrectomy for gastric ulcer is usually followed by anacidity, whereas after duodenal ulcer only 25 per cent become anacid.

SUMMARY

1. In the dog atropine in nontoxic doses (1 to 1.5 mg.) can abolish the secretion of hydrochloric acid produced by food in the Pavlov pouch, in the Haidenhain pouch and in transplanted subcutaneous gastric pouches without the myenteric plexus.

2. In the latter type of pouch the parasympathetic (vagi) and the preganglionic and postganglionic sympathetic nerves are eliminated. Whether the postganglionic parasympathetic nerves are also absent cannot be stated until the relations of the submucous plexus are definitely known.

3. At any rate, following food, only stimuli through the blood could reach this pouch. These stimuli could be completely eliminated by 1 mg. of atropine.

4. The method by which the humoral secretion from food is inhibited by atropine in the transplanted pouches is not clear. This action may take place either in the antrum or peripherally at the cells.

5. One milligram of atropine does not abolish the secretion of 1 cc. of histamine in these pouches. The histamine probably acts directly on the cell.

6. The same dose of atropine that could abolish stimulation by food when given fifteen minutes before a meal was ineffectual when given after a meal. This fact may be of use clinically.

7. In one dog with a transplanted pouch a spontaneous secretion was present at irregular intervals not associated with the test meal. This secretion was diminished by 1 mg. of atropine, but was not abolished. When it was present and a test meal was given, the atropine did not abolish the secretion. This spontaneous secretion could not have been due to vagus stimulation. It is possible that it was of parenteral origin and that its action was directly on the cell.

8. In man atropine apparently does not abolish the chemical phase of secretion. The differences and possible causes are briefly discussed.

22. Klein, E.: Gastric Secretion After Partial Gastrectomy, J. A. M. A. **89**: 1235 (Oct. 8) 1927.

9. It is possible that variations in the proportionate amount of the primary (cephalic) and secondary (chemical) phases of secretion partly account for (1) the lower acidity in gastric ulcers as compared to duodenal and (2) the far higher percentage of anacidity following partial gastrectomy for gastric ulcer. If in gastric ulcer a larger proportion of the secretion is due to the chemical phase from the antrum, the removal of this part of the stomach would account for the greater frequency of the anacidity.

ETIOLOGY OF GALLSTONES

III. EFFECT OF DIET ON THE BILE SALT-CHOLESTEROL RATIO

L. E. DOSTAL, M.D.
AND
EDMUND ANDREWS, M.D.
CHICAGO

It has been shown by us in previous papers [1] that the actual cholesterol content in the bile is not so important in gallstone formation as the ratio of the cholesterol to the substance that holds it in solution, that is, the bile salts. Therefore, it becomes important to study the factors influencing this ratio. The single factor of the concentration of the cholesterol and of the bile salts taken separately have each received much previous attention, and there is a large literature on the subject which it is not necessary to review here. However, the important factor of simultaneous estimation of the two substances has rarely been employed, and the following studies are an attempt to fill this gap. This paper will be mostly concerned with the cholesterol factor in this ratio and with attempts to vary bile cholesterol by the administration of fat or lipoids. The literature on the biliary excretion of cholesterol is rather extensive, and the results reported are apparently so contradictory that before presenting our own data, a critical review is necessary.

The earliest work of importance on this subject was done in Naunyn's laboratory in Strasbourg in the early nineties. Naunyn believed that gallstones originated in the secretion of the mucosa of the gallbladder, and the following three sets of experiments were done under his direction. Jankau [2] used both dogs and rabbits in his experiments, making biliary fistulas and estimating the cholesterol content of the fistula bile under various conditions of feeding. He found that the administration of enormous amounts of cholesterol in oil (5.5 Gm.),

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From the Department of Surgery, University of Chicago.

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1. Andrews, E.; Schoenheimer, R., and Hrdina, L.: Etiology of Gallstones: I. Chemical Factors and the Rôle of the Gallbladder, Arch. Surg. **25**:796 (Oct.) 1932. Andrews, E.; Hrdina, L., and Dostal, L. E.: Etiology of Gallstones: II. Analysis of Duct Bile from Diseased Livers, Arch. Surg. **25**:1081 (Dec.) 1932.

2. Jankau, L.: Ueber Cholesterin und Kalkausscheidung mit der Galle, Arch. f. exper. Path. u. Pharmakol. **19**:237, 1891.

either subcutaneously or by mouth, caused no rise in the biliary cholesterol. Examination of the intestine or the area of injection showed that the cholesterol had disappeared. Intraduodenal injections led to similar results. Thomas,[3] also using both dogs and rabbits with biliary fistulas, studied the effect of diets of meat, bread or fat, and likewise found no changes in the biliary cholesterol in a considerable series. Kausch [4] performed feeding experiments with negative results, and also analyzed the bile from cadavers in many diseases and found no significant increase in any. These experiments led Naunyn [5] to conclude that the cholesterol content of bile was independent of any alimentary influences, and not related to the blood cholesterol or any disease process.

The work cited has been questioned on several grounds. In the first place it was done before any modern chemical methods for accurate cholesterol estimation were devised. This is undoubtedly true and, furthermore, the figures given are in many cases quite outside the range that later observers with better methods have found in similar fluids. It must be admitted, however, that considering the methods available the work seems remarkably accurate, and while the absolute values may not be correct, the lack of change in the relative values cannot be so lightly dismissed.

Little work was done on the subject for about twenty-five years; then the introduction of the Lieberman-Burchard colorimetric method of estimation of cholesterol in small amounts of blood gave rise to many further investigations. Naunyn's views of gallstones as resulting from catarrh of the gallbladder were discarded, and the exact opposite, the theory of "cholesterol diathesis," supplanted them. It was reasoned that a high blood cholesterol implied a high bile cholesterol, and gallstones were thus easily explained. An enormous volume of papers were published on this subject for the next ten years. These need not be enumerated here; it is sufficient to say that the more careful workers found no evidence of raised blood cholesterol with gallstones in the absence of biliary obstruction. One of us (E. A.) made 250 such estimations in 1916-1917, and was quite disappointed to find no correlation whatsoever. It was not until 1924, however, that the elaborate and careful studies of Campbell [6] finally and conclusively laid the ghost of this theory by showing that the average patient with gallstones had a

3. Thomas: Ueber Abhängigkeit der Absonderung und Zusammensetzung der Galle von der Nährung, Dissert., Strasbourg, 1890.

4. Kausch: Ueber den Gehalt der Leber an Galle und Cholesterin, Dissert., Strasbourg, 1891.

5. Naunyn, B.: A Treatise on Cholelithiasis, London, New Sydenham Society, 1896.

6. Campbell, J. M. H.: Cholesterol in Blood in Cases of Gall-Stones, Quart. J. Med. **18**:123, 1924.

normal amount of blood cholesterol. Not only Campbell's own work but his careful review of the subject is important.

In the meantime sporadic papers had appeared on the relation of blood cholesterol to bile cholesterol. In 1907 Goodman [7] showed that the destruction of erythrocytes in vivo raised the cholesterol of the blood, and Kusumoto's [8] careful work on the bile in animals poisoned with tolylenediamine (a strongly hemolytic agent) showed a large increase in the cholesterol excreted in the bile. This work is not open to criticism from a chemical standpoint, but the interpretation put on it by other workers is, in our opinion, totally unwarranted. The blood cholesterol in ordinary normal or pathologic persons is certainly not to be compared to that loosed by disintegration of red cells by poisons. While a part of our blood cholesterol may, without doubt, have such an origin, it certainly is but a small part, as this would imply a much faster normal replacement than actually takes place. Such experiments are surely not to be taken as proof that a high blood cholesterol implies a high bile cholesterol in general.

Bacmeister [9] studied the bile in diabetic patients with fistulas, and concluded that the cholesterol averaged higher than in normal persons. The differences he found were, however, not far outside the normal limits when the marked variability of biliary cholesterol is taken into consideration. This work has been cited by McNee as evidence of a relation of bile and blood cholesterol, although Bacmeister himself concluded that his results were secured "nicht allein durch die verschiedene Nährungsform erklären lassen [not only through the different forms of diet explained]." In two diabetic patients coming under our observation the cholesterol in fistula bile was within normal limits. In one of these a twenty-four hour sample was possible, and it also was normal. (Experimental studies on this subject are being undertaken.)

Peirce [10] studied the type of cholesterol in a series of human biles. He found that esters were very low and that free cholesterol made up the majority. While his work has been quoted as showing a relation between blood and bile cholesterol (e. g., in nephritic patients it was high), careful examination of his tables shows that cholesterol was even higher in other conditions not associated with hypercholesteremia.

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7. Goodman, E. H.: Ueber den Einfluss der Nährung auf die Ausscheidung von Gallensäuren und Cholesterin durch die Galle, Beitr. z. chem. Physiol. u. Path. **9**:91, 1907.

8. Kusumoto, C.: Ueber den Einfluss des Toluylendiamins auf die Ausscheidung des Cholesterins in der Galle, Biochem. Ztschr. **13**:354, 1908.

9. Bacmeister: Untersuchungen über Cholesterinausscheidung in menschlichen Gallen, Biochem. Ztschr. **26**:223, 1910.

10. Peirce, S. J. S.: Der Gehalt der menschlichen Galle in Cholesterin und Cholesterinestern, Deutsches Arch. f. klin. Med. **106**:337, 1912.

Havers'[11] experiments on dogs revealed a slight increase in the biliary cholesterol after the feeding of fat. It became less in febrile conditions and, most interesting of all, it appeared to be definitely decreased in pregnancy. The latter fact led Havers to the hypothesis that the well known hypercholesteremia of pregnancy is a retention due to the fact that not enough is excreted in the bile. Such a concept of hypercholesteremia, while it has but little evidence in its support as yet, must be kept in mind as a possibility in many other conditions besides the classic example of jaundice.

D'Amato[12] showed that the cholesterol in the bile was diminished markedly in intoxication by liver irritants. The injection of alcohol, amyl alcohol, acetic acid or butyric acid had this effect. The subcutaneous injection of Bacillus coli had a similar effect. As will be seen later, the authors have shown that ether may have a similar action, although the effect is variable.

One of the most important observations was that of Rothschild[13] in 1915. He showed that the amount of cholesterol in the blood, in the liver and, most significantly, in the bile was enormously increased by starvation. While the now well known fact of starvation lipemia is not of interest here, it would be important to get evidence of gallstone formation in such cases. Evidence for or against this to our knowledge is almost totally lacking in spite of the widespread condition during the war and postwar periods. Rothschild's observations have been confirmed by McMaster[14] and others. The interesting point is that from the standpoint of degree such changes tend to mask all others, as they are so extremely great. The biliary cholesterol may be more than tripled in a short time by starvation, and this is the only method ever reported which had led to anything approaching such concentrations. Whether the concomitant desiccation of the body with consequent concentration of the bile is adequate to explain it is doubtful. The well known starvation syndrome of edema resembling lipoid nephrosis may give rise to a much greater endogenous production of cholesterol by the breaking up of body cells and the accumulation of insoluble and slowly excreted cholesterol. In our experiments on dogs this has

11. Havers, K.: Experimentelle Untersuchungen über Physiologie und Pathologie des Cholesterinstoffwechsels mit besonderer Berücksichtigung der Schwangerschaft, Deutsches Arch. f. klin. Med. **115**:267, 1914.

12. D'Amato, L.: Chemische Veränderungen der Galle bei Leberintoxikationen und ihre Wichtigkeit in der Pathogenese der Gallensteinkrankheit, Biochem. Ztschr. **69**:353, 1915.

13. Rothschild, M. A.: Zur Physiologie des Cholesterinstoffwechsels: V. Der Cholesteringehalt des Blutes und einiger Organe im Hungerzustand, Beitr. z. path. Anat. u. z. allg. Path. **60**:227, 1915.

14. McMaster, P. D.: Studies on Total Bile, J. Exper. Med. **40**:25, 1924.

often served to mask other, smaller changes, and it is to be constantly kept in mind in any studies on this subject, as it has been a fertile source of error.

McNee [15] studied the gallbladder bile in pregnant women dying of septic abortion and found its cholesterol content higher than normal. From this he concluded that the hypercholesteremia of pregnancy was accompanied by an increase in the bile cholesterol.[16] This conclusion is open to grave question. In the first place, the agonal changes in the liver and the obvious antemortem starvation in such cases make it rather doubtful if postmortem material of this type can apply to the normal pregnant woman. Again, there is a tendency, which we have noted previously,[17] for the gallbladder to concentrate dilute biles to somewhat the same concentration as normal biles. The concentrating process tends to continue until the total solids reach the level of about 25 per cent. This view of McNee's has received more widespread notice in his summary of the knowledge of cholesterol metabolism, and again in Rolleston and McNee's "Diseases of the Liver, Gall Bladder and Bile Ducts." [18]

Further support was given to these theories by Stepp,[19] who reported a slight decrease (from 10 to 15 per cent) in the bile cholesterol in animals on a lipoid-free diet. This seems a rather small change on which to base any conclusions in a field in which the normal, uncontrolled variations are ten times as great. Pribrams' [20] studies on the bile of pregnant women yielded much more striking results. He found that during the first months of pregnancy the cholesterol content of the bile was low but later reached excessively high figures which persisted for a considerable period after delivery. His figures showed a degree of change far beyond the possibility of experimental error. However, his specimens were derived by duodenal intubation, and the liver bile and gallbladder bile were fractioned according to the Meltzer-Lyon technic. He believed that he was correct in stating that not one clinician in ten today has any confidence that specimens obtained in this manner can be definitely assigned any origin. Secondly, as will be shown, most of the

15. McNee, J. W.: Zur Frage des Cholesteringehalts der Galle während der Schwangerschaft, Deutsche med. Wchnschr. **39**:994, 1913.

16. McNee, J. W.: Cholesterin, an Account of Its Relations to Pathology and Physiology, Quart. J. Med. **7**:221, 1914.

17. Andrews, Schoenheimer and Hrdina (footnote 1, first reference).

18. Rolleston, R., and McNee, J. W.: Diseases of the Liver, Gall Bladder and Bile Ducts, ed. 3, London, The Macmillan Company, 1920.

19. Stepp, W.: Beobachtungen über den Cholesteringehalt des Blutes und der Galle bei Lipoidfrei ernährten Thieren, Ztschr. f. Biol. **69**:514, 1919.

20. Pribram, E. C.: Zur Frage des Cholesterinstoffwechsels während der Schwangerschaft und im Wochenbett, Arch. f. Gynäk. **120**:90, 1923.

intestinal sterols are not biliary in origin. These two facts, to our mind, completely vitiate the results of this work.

The most recent study on this subject has been the reports of a series of English investigators, whose results substantiate the theory that ingested cholesterol does not appear in the bile. Fox,[21] in a carefully controlled series of studies, was not able to demonstrate the slightest effect of diet. Gardner and Gainsborough,[22] in their masterly review of cholesterol metabolism, stated that they did not believe that biliary cholesterol can be affected by diet. Gainsborough,[23] in a study of so-called lipoid nephrosis in which the blood cholesterol reached very high levels, found normal amounts in the bile.

Finally come the elaborate studies of Peyton Rous and his associates, which were reviewed by us in a previous paper. These studies were done in the only really scientific manner, as they used the two-way fistula of McMaster,[24] so that the bile after sampling was returned to the intestine. Their results showed a slight rise from diets rich in cholesterol, but an increase in the cholesterol of the bile from starvation which overshadowed all other influences.

To show the absurdity of much of the previous work on the subject, it is only necessary to call attention to the fact that it was done utilizing complete biliary fistulas from either the clinic or the experimental laboratory. It has repeatedly been shown in such cases that all fatty material passes through the gastro-intestinal tract unchanged under such circumstances and can be recovered quantitatively in the stools. The evidence on this subject was summed up by Gardner and Gainsborough.[22] The futility of feeding experiments under such conditions is obvious. Added to this, it is interesting to note the crucial experiments of Schoenheimer,[25] showing that plant sterols are not absorbed at all.

It is a common misapprehension that most of the fecal sterols are biliary in origin. Since the early experiments of Voit [26] in 1892 it has been known that the mucosa of the gastro-intestinal tract secretes much lipoid material. This is not lessened, but on the contrary markedly

21. Fox, F. W.: The Composition of Human Bile and Its Bearing upon Sterol Metabolism, Quart. J. Med. **21**:107, 1927.

22. Gardner, J. A., and Gainsborough, H.: Blood Cholesterol Studies in Biliary and Hepatic Diseases, Quart. J. Med. **23**:465, 1930.

23. Gainsborough, H.: A Study of So-Called Lipoid Nephrosis, Quart. J. Med. **23**:101, 1929.

24. McMaster, P. D., and Elman, R.: Studies on Urobilin Physiology and Pathology: II. Relation of Bile to the Presence of Urobilin in the Body, J. Exper. Med. **41**:513, 1929.

25. Schoenheimer, R.: Ueber die Bedeutung der Pflanzensterine für der tierischen Organismus, Ztschr. f. physiol. Chem. **180**:1, 1929.

26. Voit, F.: Beiträge zur Frage der Secretion und Resorption im Dünndarm, Ztschr. f. Biol. **11**:325, 1892.

increased, if the bile is side-tracked by a biliary fistula. In the classic experiments of Sperry [27] on sterol absorption he found that from one and a half to four and a half times as much sterol was present in dog's stools if the bile was drained externally and a lipoid-free diet given. These observations have been amply confirmed and extended by Buerger and Oeter [28] and also by Beumer and Hepner.[29] The latter authors believe that the amount of biliary cholesterol in the stools makes up but a small part of the total. It has long been known that most of the stool cholesterol is a hydrogenated sterol, coprosterol. This is not resorbed. Whether it is hydrogenated before or after excretion is a questionable point. The biliary cholesterol may be absorbed or hydrogenated to the nonresorbable coprosterol in the intestine. The latter possibly takes place from the action of intestinal bacteria. Schoenheimer [30] has demonstrated a large excretion of sterols by the isolated colon of dogs. Similar studies of the secretion of blind loops of the small intestine also yield high sterol contents.[31]

With these points in mind, one must admit that, while the effect of diet or hypercholesteremia on the biliary cholesterol as a factor in gallstone formation cannot yet be said to be settled, the weight of evidence lies on the negative side. The following experimental and clinical observations tend in our opinion to substantiate this view.

EXPERIMENTAL WORK

Studies were first made on dogs, using the two-way fistula described previously by Peyton Rous and his associates. It is important that such a fistula be used in all of these experiments, as not only does simple drainage of the bile cause infection of the liver and hence disturbance in its physiologic action, but the absence of bile in the intestine breaks up the enterohepatic circulation described by Whipple,[32] and the previous work on this subject which was done in a single one-way fistula may be said to have very little value, for our purposes at least.

While it has long been known that absence of bile from the bowel prevents the absorption of fat, the studies of Weiland and Sorge [33]

27. Sperry, W. M.: Lipoid Excretion: IV. A Study of the Relationship of Bile to the Fecal Lipoids with Special Reference to Certain Problems of Sterol Metabolism, J. Biol. Chem. **71**:351, 1926-1927.

28. Buerger, M., and Oeter, H. D.: Ueber den Cholesteringehalt der menschlichen Darmwand, Ztschr. f. physiol. Chem. **182**:141, 1929.

29. Beumer, H., and Hepner, F.: Ueber die Ausscheidungswege des Cholesterins, Ztschr. f. d. ges. exper. Med. **64**:787, 1929.

30. Schoenheimer, R., and von Bedring, H.: Ueber die Exkretion gesättigter Sterine, Ztschr. f. physiol. Chem. **192**:102, 1930.

31. Schoenheimer, R.: Unpublished work.

32. Whipple, G. H.: Bile Salt Metabolism, J. Biol. Chem. **59**:623, 1924.

33. Weiland, H., and Sorge, H.: Untersuchungen über die Gallensäuren, Ztschr. f. physiol. Chem. **97**:1, 1916.

perhaps give a more complete explanation of the phenomenon. They showed that desoxycholic acid has the power to make loose chemical compounds with a number of different fatty acids. The absorption of fat, it has been suggested, may take place by some such mechanism, and therefore the absence of bile acids from the intestine stops this method of rendering these substances soluble.

The two-way fistula that leads from the proximal end of the common duct to the outside, where it may be tapped and specimens secured, and then goes back to the distal end of the common duct has proved in our hands exceedingly difficult to keep in working condition for long periods. However, with care it can be done, and the accompanying tables are illustrations of the results of such studies.

TABLE 1.—*Effect of Diet on the Bile Cholesterol of Dog 223* *

			Cholesterol, Mg. per 100 Cc.	Bile Salts, Mg. per 100 Cc.	Ratio of Bile Salts to Cholesterol
	5/ 6/31	Gallbladder specimen removed at operation	68.18	4796.5	70.5
1	5/ 6/31	Immediate postoperative specimen.....	27.0	588.2	21.7
2	5/ 7/31	Fed ordinary meat diet; then drained for 4 hours	11.7	269.1	23.0
3	5/ 8/31	Fed ordinary meat diet; then drained for 4 hours	41.6	1063.37	25.5
4	5/ 9/31	Given 100 cc. olive oil by stomach tube; then drained for 4 hours	19.7	1425.4	72.3
5	5/11/31	Given 100 cc. olive oil and 100 cc. cream by tube; then drained 4 hours	21.8	1312.2	60.1
6	5/12/31	Given 100 cc. cream; then drained for 4 hours	10.5	1221.7	116.3
7	5/18/31	Fed 2 Gm. bile salts; then drained for 4 hours	21.4	1380.0	64.4
8	5/19/31	Fed 2 Gm. bile salts; then drained for 4 hours	21.1	1561.0	74.0

* The two-way fistula of McMaster was used, the bile being returned to the bowel after sampling.

DOG 223 (table 1).—The points to be noted here are: First, the wide fluctuations in the cholesterol content in the bile here were due to entirely extraneous influences. The first postoperative specimen taken when the liver was still under the influence of the anesthetic throughout our series showed wide fluctuations in both man and animals. In two cases in human beings reported in a previous paper [34] the cholesterol under these conditions was exceedingly low, falling almost to zero. This was true in some of our dogs, and again in others it tended to run unusually high. We suggest the possibility that dehydration due to operative hemorrhage may have been a factor. The important thing, however, to be noted is the fact that the administration of large amounts of fat has certainly not given the effect of increasing the bile cholesterol. Meat, regarded by some as a precursor of cholesterol, also had no effect. This has been true through our series. In the latter part of the

34. Andrews, Hrdina and Dostal (footnote 1, second reference).

experiment very large amounts of bile acids were fed by mouth, and these also produced no apparent effect on either the cholesterol or the bile acid content of the bile, both of which remained within normal physiologic limits. It was thus possible that the presence of larger amounts of bile acid in the intestine hastened the absorption of cholesterol, which may indeed be the case although it is not reflected in an increased biliary cholesterol. Unfortunately, no studies of the blood cholesterol were made concurrently. The bile salt-cholesterol ratio in

TABLE 2.—*Effect of Diet on the Bile Cholesterol of Dog 167* *

		Cholesterol, Mg. per 100 Cc.	Bile Salts, Mg. per 100 Cc.	Ratio of Bile Salts to Cholesterol	Calcium, Mg. per 100 Cc.
4/15/31	Immediate postoperative specimen.....	15.9	828.21	51.8	5.0
4/16/31	No food postoperatively; bile drained for 4 hours	13.5	757.0	44.6	7.4
4/17/31	Olive oil, 250 cc., by stomach tube; then drained for 4 hours	20.0	1078.0	53.0	5.8
4/20/31	A.m.: dog fasting; drained for 4 hours.....	36.5	1439.0	39.0	12.5
4/20/31	P.m.: 500 Gm. bread and 100 cc. Karo syrup; drained for 4 hours	54.5	858.3	15.0	6.75
4/21/31	Fed 500 Gm. lean meat; drained for 4 hours.....	31.5	1391.0	44.0	12.6
4/22/31	No feeding; bile drained for 4 hours.....	18.0	1357.0	74.0	13.9
4/24/31	No feeding; bile drained for 4 hours.....	7.4	1123.0	150.0	....
4/24/31	Olive oil, 300 cc., by stomach tube; drained for 4 hours	8.6	532.0	62.0	8.8

* The two-way fistula of McMaster was used, the bile being returned to the bowel after sampling.

TABLE 3.—*Effect of Diet on the Bile Cholesterol of Dog 180* *

		Cholesterol, Mg. per 100 Cc.	Bile Salts, Mg. per 100 Cc.	Ratio of Bile Salts to Cholesterol	Calcium, Mg. per 100 Cc.
4/22/31	Immediate postoperative specimen.....	9.5	939.5	98.6	11.45
4/23/31	No feeding; bile drained for 4 hours.....	12.5	689.9	55.2	12.7
4/24/31	A.m.: stock diet fed the night previously; drained for 4 hours	8.0	158.8	79.4	9.2
4/24/31	P.m.: 300 cc. olive oil by stomach tube; drained for 4 hours	10.0	527.3	52.7	9.4
4/25/31	Stock diet fed the night previously; drained for 4 hours	18.4	.....	....	....

* The two-way fistula of McMaster was used, the bile being returned to the bowel after sampling.

dog liver bile runs from 50 to 150, averaging around 100. During the first postoperative day or two the ratio as shown here was quite low, lying in the range of normal levels in human beings. However, we attached no significance to this fact whatsoever, as it was shown in a previous paper that under influences of liver poisons much of the bile acids is excreted in an uncombined form which would not show in the amino-nitrogen method of Van Slyke, which was used throughout.[34]

DOG 167 (table 2).—The same features were obvious throughout this experiment. There was no effect whatsoever from the administration of fatty foods. In fact, the lowest bile cholesterol found was after

the administration of large amounts of olive oil. Here again a factor is evident that McMaster [14] had noted; that is, that the biliary cholesterol is raised by starvation far more than by any other means. The bile salt-cholesterol ratio runs in the usual range except during the first few days after operation, when it is apparently disturbed by the factors already mentioned.

Dog 180 (table 3).—Here again the total dissociation of fatty food from bile cholesterol is obvious, and the bile salt-cholesterol ratio remained within the normal limits for this type of animal throughout the experiment.

Table 4 is put in simply to show cholesterol values in postoperative specimens and well illustrates the wide variation found in these early

TABLE 4.—*Early Postoperative Bile Cholesterol: the Effect of Ether*

Rous Double Fistulas		Mg. of Cholesterol per 100 Cc. of Bile
Dog 177	First postoperative specimen	14.2
	Second postoperative specimen	22.0
	Third postoperative specimen	33.3
		42.1
Dog 232	First postoperative specimen	28.0
Dog 293	First postoperative specimen	14.2
	Second postoperative specimen	23.0
Dog 281	First postoperative specimen	10.7
Case 9658	(Human being)	8.40
Case 34963	(Human being)	48.0
Case 36958	(Human being)	4.73

specimens. Whether it is related to starvation or not is difficult to tell, but it is a fact that in certain cases following operation bile containing an unusually large amount of cholesterol may be excreted.

CLINICAL DATA

Table 5 is illustrative of a carefully controlled experiment on a human being with a common duct tube from which all the bile was drained; the observations were continued for nineteen days. This is the same case part of the data from which was reported in the second paper of this series.[1] The patient had diabetes of mild degree, well controlled before operation. During the first few days after operation she had a slight glycosuria with some acidosis, but she rapidly returned to normal and was able to eat a normal diet during the last fourteen days of the experiment. While unfortunately no studies were made on the blood cholesterol, one would certainly expect somewhat of a lipemia in such a case. It is obvious from the chart and table 5 that if this was present it was not reflected by increased excretion in the bile.

The diet was rapidly increased to normal on the first four postoperative days, and from then on the patient received 130 Gm. of fat per day. On the twelfth to fifteenth day this diet was cut down to 50 Gm. of fat per day, and again it can be seen that this had no effect on the biliary cholesterol. During each of the periods noted she had

TABLE 5.—*Complete Record on Fistula Bile in Patient E. C.*

No.	Time	Volume, Cc.	Total Solids, Gm.	Calcium, Mg. per 100 Cc.	Cholesterol, Mg. per 100 Cc.	Bile Salts as Glycocholate, Mg. per 100 Cc.	Comment
1	1st postoperative hr.	15	3.54	6.45	48.0	6	
2	Next 18 hours	250	3.43	7.7	58.8	47	
3	8 a.m. to 4 p.m.	46	1.99	6.0	50.0	0	
4	4 p.m. to 12 a.m.	95	1.98	5.35	51.2	0	
5	12 a.m. to 8 a.m.	108	1.79	4.6	47.5	0	
6	8 a.m. to 4 p.m.	124	1.50	4.7	48.1	6	
7	4 p.m. to 8 a.m.	158	2.13	4.1	54.5	0	
8	8 a.m. to noon	28	2.11	5.0	62.4	22	8 a.m.: dehydrocholic acid, 0.5 Gm.
9	Noon to 8 a.m.	145	2.80	5.35	82.1	29	
10	8 a.m. to noon	15	....	7.34	62.4	35	8 a.m.: desoxycholic acid, 0.5 Gm.
11	Noon to 8 a.m.	200	2.43	7.1	52.8	57	
12	8 a.m. to noon	20	....	7.7	50.8	44	8 a.m.: dehydrocholic acid, 0.5 Gm.; cholesterol, 1 Gm.
13	Noon to 8 a.m.	180	3.46	7.5	65.0	13	
14	8 a.m. to noon	45	2.62	6.9	58.0	42	
15	Noon to 8 a.m.	200	3.47	7.9	73.0	51	
16	8 a.m. to noon	60	3.99	7.1	69.0	0	
17	Noon to 8 a.m.	500	2.10	6.2	83.0	20	
18	8 a.m. to noon	45	2.56	7.2	51.0	66	8 a.m.: desoxycholic acid, 0.5 Gm.; cholesterol, 1 Gm.
19	Noon to 8 a.m.	200	3.38	8.3	81.0	47	
20	8 a.m. to noon	30	....	8.3	58.0	103	8 a.m.: dehydrocholic acid, 0.5 Gm.
21	Noon to 8 a.m.	195	2.98	6.9	75.0	22	
22	8 a.m. to noon	45	3.16	8.7	56.0	70	8 a.m.: dehydrocholic acid, 0.5 Gm.
23	Noon to 8 a.m.	260	3.37	6.9	83.0	72	
24	8 a.m. to noon	150	2.49	8.3	67.0	42	8 a.m.: dehydrocholic acid, 0.5 Gm.; cholesterol, 1 Gm.
25	Noon to 8 a.m.	350	2.44	7.1	56.0	46	
26	8 a.m. to noon	105	2.82	6.8	76.0	11	8 a.m.: cholesterol, 1 Gm.
27	Noon to 8 a.m.	355	2.50	6.7	66.0	46	
28	8 a.m. to noon	125	2.41	5.5	60.0	18	8 a.m.: cholesterol, 1 Gm.
29	Noon to 8 a.m.	415	2.45	7.1	58.0	25	
30	8 a.m. to noon	65	2.92	7.9	71.0	32	8 a.m.: cholesterol, 1 Gm.
31	Noon to 8 a.m.	550	2.72	6.6	67.0	45	
32	8 a.m. to noon	150	2.05	5.6	58.0	0	8 a.m.: cholesterol, 1 Gm.
33	Noon to 8 a.m.	445	2.08	5.5	71.0	15	
34	8 a.m. to noon	125	2.35	5.5	49.0	0	
35	Noon to 8 a.m.	350	2.50	6.0	78.0	11	
36	8 a.m. to noon	75	2.35	5.3	57.0	11	
37	Noon to 8 a.m.	365	2.50	5.9	63.0	11	
38	8 a.m. to noon	140	1.92	4.6	62.0	11	
39	Noon to 8 a.m.	325	2.41	4.7	65.0	0	

received doses of bile salts by mouth which should have aided in the absorption of fat.

During the course of the experiment, cholesterol was administered by mouth on various occasions, as were bile acids and both substances together. In each case these were given at 8:00 a. m., and the subsequent four hour specimen of bile was analyzed separately from the rest of the twenty-four hour specimen. During the entire period here

reported the stools were free from bile. The cholesterol was dissolved in butter which was allowed to harden again before feeding. This is quite necessary, as crystalline cholesterol is often not absorbed. The dose in each case was 1 Gm. The bile acids used were desoxycholic and dehydrocholic, in doses of 0.5 Gm. in several capsules. It is important to use the acids and not the sodium salts, which are much more disagreeable to taste. The patient was afebrile during the experiment, and was able to take fluids freely, so that dehydration was not a factor. All the ingested food and drugs were retained, there being no vomiting.

The data gathered in the studies may be summarized as follows:

1. As already noted, the fact that the patient had diabetes did not bring about an increase in the amount of cholesterol in the bile either in the concentration or in the daily output.

2. Variations in the dietary fats and proteins had no effect on the biliary excretion. While it has been noted by various observers [35] that the blood cholesterol is affected by diet only slowly and over long periods, one would expect a nineteen day study of this type to have some effect on the bile, even allowing for the slowness of the response.

3. The feeding of cholesterol, even when accompanied by bile acids, likewise had no effect whatsoever.

4. The feeding of bile acids, desoxycholic or dehydrocholic, either alone or with cholesterol, had no effect on the bile cholesterol. Theoretically these must have materially hastened the absorption of fats and raised the blood cholesterol, and we regret that this was not studied.

5. No correlation between the cholesterol and the total solids of the bile could be found.

6. No relation existed between the cholesterol content and the volume of bile excreted.

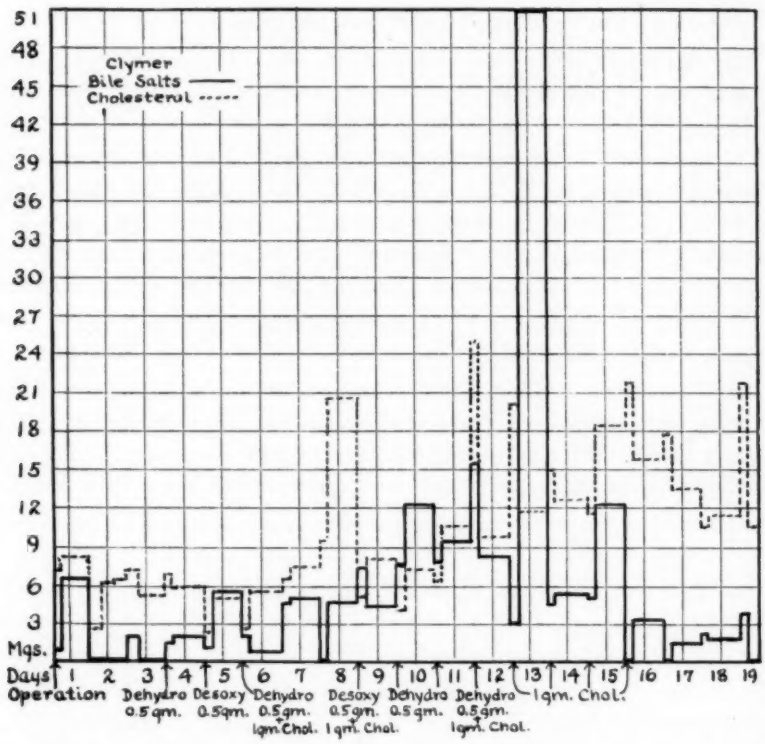
7. The constancy of the bile cholesterol here as well as in other experiments in human beings previously reported is remarkable. In this case in spite of all the changes in the experimental conditions, it varied only between 55 and 75 mg. per hundred cubic centimeters. In our hands the colorimetric estimation has never been perfected to the same degree of accuracy reported by several other observers. With our most carefully made tests the margin of error has proved to be at least 15 per cent. From this it may be seen that the fluctuations within the range reported may be mostly experimental error. In dogs the range of normal fluctuation is often much greater than in man.

The accompanying chart is composed of the same data plotted to represent in milligrams per hour the excretion of both bile salts and

35. Fox (footnote 21). Gardner and Gainsborough (footnote 22). Gainsborough (footnote 23).

cholesterol. When plotted in this manner it is evident at once that the fluctuations are considerably greater. However, careful examination of the chart again confirms the fact that there is no correlation whatsoever between the excretion per hour of cholesterol and (1) diet, (2) the oral administration of cholesterol and (3) the oral administration of bile acids.

After a postoperative period with very small cholesterol excretion, it reaches a level which it tends to maintain entirely free from dietary



Same data as tabulated in table 5, calculated in milligrams per hour. Note the complete dissociation of the diet and feeding of cholesterol or bile salts from the excretion of either in the bile.

influence. One of the most striking phenomena noted was the fact that the cholesterol excretion was so much higher in the morning specimens throughout. It averaged 18 mg. per hour, and then 12 mg. per hour during the rest of the day, a 50 per cent increase. Fasting is probably the explanation of these results. The total cholesterol found in the bile during the last ten days of the experiment, after the postanesthetic period was over, was only about 3 Gm. This is in marked contrast to

the fact that the patient received 6 Gm. of pure cholesterol by mouth besides the considerably larger amount that was contained in the high fat diet given for diabetes. This appears to confirm in man the observations of Schoenheimer on dogs, that the major share of cholesterol is excreted by the mucosa of the bowels. It is unthinkable that such a large amount is stored daily, even with a bile fistula. Of course, it may be that the meager amount of bile salts provided (3.5 Gm.) was not enough to permit the absorption of so much lipoid material.

COMMENT

Gardner and Gainsborough,[22] in their recent studies on blood cholesterol, not only agreed with Campbell in totally dissociating it from the problem of gallstone formation [6] but also showed that the previous conceptions of biliary obstruction and cholesterol were at fault. They quite conclusively demonstrated that in biliary obstruction there is not a rise but a marked fall in the sterol content of the blood. This fall, which also occurs after fistula formation, is in the ester fraction and is due to failure of absorption from the intestine. It is only after prolonged jaundice that a rise in the blood cholesterol occurs. The following quotations from their conclusions is quite in accord with our findings:

> The usual theory that this change is due to retention in the blood of cholesterol from the bile is quite inadequate. . . . Hypercholesterolemia does not occur in uncomplicated cholelithiasis. . . . There is no evidence that the cholesterol content of the food influences the cholesterol content of the bile or has any relation to gall stone formation. . . . The marked hypercholesterolemia, which occurs in some forms of nephritis, also does not lead to any increase in incidence of cholelithiasis.

CONCLUSIONS

1. The cholesterol content of the bile is independent of dietary factors.

2. In these studies no changes in the bile salt-cholesterol ratio of sufficient magnitude to approach the critical level for precipitation have been found. The responsibility for gallstone formation seems to lie in the gallbladder rather than the liver.

HEALING OF FRACTURES, OF DEFECTS IN BONE AND OF DEFECTS IN CARTILAGE AFTER SYMPATHECTOMY

J. ALBERT KEY, M.D.
ST. LOUIS
AND
ROBERT M. MOORE, M.D.
GALVESTON, TEXAS

In this article we wish to report the results of experiments performed in an attempt to determine whether or not sympathectomy influences the healing of cartilage and bone.

HEALING OF FRACTURES AND OF BONE DEFECTS AFTER SYMPATHECTOMY

The Literature.—Physiologists have demonstrated repeatedly that removal of the sympathetic ganglions supplying a limb is followed by a dilatation of the blood vessels and increased flow of blood through that limb. Furthermore, certain investigators have maintained that an identical result is secured by the removal of a segment of the outer coat of the main artery. These developments have led clinicians to the use of one or another of these procedures in the treatment of almost every pathologic condition that might possibly be attributed to a deficiency in local circulation. One of these conditions is the state of delayed union or nonunion in fractures of the bones of the extremities.

The first use of sympathectomy in the treatment of delayed union of fractures was by Kappis [1] in 1923. He performed periarterial sympathectomy of the femoral artery of a man, aged 23, who had had a fracture of both bones of the leg about ten weeks before. The fracture had been treated by open reduction followed by skeletal traction and a plaster cast. The periarterial sympathectomy was followed by rapid union, and the fracture was healed within six weeks after the operation on the artery. In 1924, Füth [2] reported two similar cases, and two more cases were reported by Rubaschow [3] in 1925. Other cases of the same

From the Department of Surgery of Washington University, St. Louis, and of the Medical Branch of the University of Texas, Galveston, Texas.

1. Kappis, Max: Further Experiences with Periarterial Sympathectomy in Delayed Union, Klin. Wchnschr. **2**:1441, 1923.

2. Füth: Ber. a. chir. Gesellsch., November, 1924, p. 61.

3. Rubaschow, S.: Periarterial Sympathectomy in Delayed Union of Fractures, Zentralbl. f. Chir. **52**:635, 1925.

type have been reported by Gaudier,[4] Fontaine,[5] Stropeni,[6] Estor [7] and Floresco.[8] Uffreduzzi [9] made the statement that in delayed union when the delay is not due to mechanical influences, the indication for periarterial sympathectomy is perfect.

It is to be noted that all of the foregoing observations are in clinical cases, and that, with the exception of Fontaine, no author reported more than three cases. Fontaine reported eight cases, and in four of these sympathectomy appears to have been followed by definite benefit, while in four others there was no apparent benefit from the operation. In fact, in one case a low grade infection seems to have been aggravated.

Palma [10] reported experimental work in which he removed the lower cervical sympathetic ganglion on one side and fractured the radius on both sides in six rabbits. The animals were killed on the fifth, tenth, fifteenth, twentieth, thirtieth and forty-fifth days. Roentgen and microscopic examination of the fractures showed much more rapid consolidation of the fractures and disappearance of the callus in the sympathectomized limb. He believed that the more rapid union on the sympathectomized side was due to the increased blood flow in the area and considered his experimental results as proof of the importance of the blood supply in the repair of fractures. Fontaine [5] performed bilateral osteotomies of the metatarsals of dogs and periarterial sympathectomy on one side and noted more rapid union on the sympathectomized side. Gaudier [4] performed experimental periarterial sympathectomy in dogs and reported that in spite of the difficulty of the operation on small vessels there was more rapid healing in fractures of limbs that had been subjected to the sympathectomy. Unfortunately, Gaudier does not give the details of his experiments. Pearse and Morton [11] removed the sympathetic ganglions and chain from the renal vein down to the sacrum on the left side in ten dogs and resected uniform segments of the fibulae in the same animals. They were able to detect little, if any,

4. Gaudier, H.: Periarterial Sympathectomy and Fractures of the Extremities, Bull. et mém. Soc. nat. de chir. **52**:1190, 1926.

5. Fontaine, R.: Eight Cases of Retarded Consolidation and Pseudarthrosis Treated by Periarterial Sympathectomy, Rev. de chir. **64**:95, 1926.

6. Stropeni, L.: Periarterial Sympathectomy to Promote Healing of Fractures, Arch. ital. di chir. **15**:601, 1926.

7. Estor, E.: Sympathectomy and Fractures of the Extremities, Bull. et mém. Soc. nat. de chir. **53**:647, 1927.

8. Floresco, A.: A Case of Pseudarthrosis of the Forearm Healed by Periarterial Sympathectomy, Rev. d'orthop. **16**:503, 1929.

9. Uffreduzzi, Ottorino: A Study of the Physiopathological and Clinical Periarterial Sympathectomy, Gaz. d. hôp. **101**:265, 1928.

10. Palma, R.: Influence of Sympathectomy on the Process of Reparation of Fractures Through Animal Experiments, Ann. ital. di chir. **4**:85, 1925.

11. Pearse, H. E., Jr., and Morton, J. J.: The Influence of Alterations in the Circulation of the Repair of Bone, J. Bone & Joint Surg. **13**:68, 1931.

difference in the healing on the two sides and concluded that the sympathetic system has little influence on osteogenesis.

Materials and Methods.—These experiments were performed on cats, and the procedure consisted of resection on the right side of the stellate (first thoracic) ganglion and the two subjacent thoracic (second and third) sympathetic ganglions. Since all of the sympathetic preganglionic fibers leave the cord to enter the chain at or below the first thoracic segment, this operation not only destroys the sympathetic components of the first and second thoracic spinal nerves, but also interrupts the sympathetic component to all cervical nerves and is thus a complete sympathectomy for the fore leg (Ranson [12]). At intervals of from one to two weeks after the sympathectomy, transverse osteotomy of the ulna of each fore leg was performed, thus giving uniform fractures on the right sympathectomized side and on the left normal side, the latter serving as a control. The animals were then killed at intervals of from nineteen to seventy-four days after the osteotomies. At autopsy, the ulna and radius were removed, examined in the gross and then fixed in formaldehyde. X-ray photographs were made, and the bones were then decalcified, sectioned, stained in hematoxylin and eosin and studied microscopically.

In addition to the foregoing, a large rectangular defect, approximately 1.5 cm. long and including approximately half of the shaft of the ulna, was created in each fore leg of one animal in which the right upper thoracic sympathetic ganglions had been removed as described.

Results.—The fractures on both the control and the sympathectomized side appeared to heal at approximately the same rate. That is, by gross examination, x-ray photographs (fig. 1) and microscopic examination we were not able to detect any difference between the healing of fractures in the sympathectomized and the nonsympathectomized extremities. The same was true of the bone defect. On microscopic examination, there appeared to be considerable vascular dilatation in the region of the fracture in some of the sympathectomized limbs, but the same was true of the vessels in the vicinity of the fractures in the control limbs of the same animals.

It is further to be noted that the operation of sympathectomy was not followed by any demonstrable difference in the bones of the extremity which were not operated on. If it is true that increased circulation leads to absorption of bone (Leriche and Policard [13]), we

12. Ranson: An Introduction to a Series of Studies on the Sympathetic Nervous System, J. Comp. Neurol. **29**:305, 1918. Ranson and Billingsley: The Superior Cervical Ganglion and the Cervical Portion of the Sympathetic Trunk, ibid. **29**:313, 1918.

13. Leriche, R., and Policard, A.: The Normal and Pathological Physiology of Bone, St. Louis, C. V. Mosby Company, 1928.

should find atrophy of all of the bones of the sympathectomized extremities. However, careful study of these bones by roentgen and microscopic examination failed to reveal any difference in density between those of the sympathectomized and the control limb.

HEALING OF CARTILAGE AFTER SYMPATHECTOMY

The Literature.—In 1927, Rowntree and Adson [14] reported observations on cases of chronic "infectious" arthritis after sympathectomy. The advisability of this operation is still *sub judice;* however, the authors believe that in certain carefully selected cases of chronic

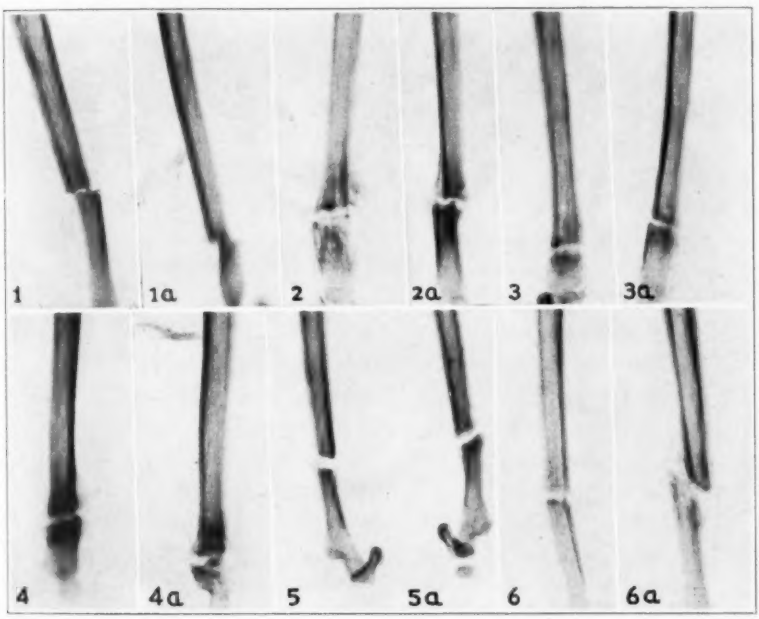


Fig. 1.—Here are shown x-ray photographs of the ulnae of cats after osteotomies (in each instance the figure on the left is from the sympathectomized limb and the one on the right is from the control): *1*, nineteen days; *1 a*, control. *2*, thirty-five days; *2 a*, control. *3*, forty-one days; *3 a*, control. *4*, fifty-one days; *4 a*, control. *5*, sixty-four days. *5 a*, control. *6*, seventy-four days; *6 a*, control.

"infectious" arthritis sympathectomy is indicated and offers a chance of considerable improvement in cases that have not responded to other forms of treatment (Hench, Henderson, Rowntree and Adson [15]).

14. Rowntree, L. G., and Adson, A. W.: Bilateral Lumbar Sympathetic Ganglionectomy and Ramisectomy for Polyarthritis of the Lower Extremities, J. A. M. A. **88**:694 (March 5) 1927.

15. Hench, P. S.; Henderson, M. S.; Rowntree, L. G., and Adson, A. W.: The Treatment of Chronic "Infectious" Arthritis by Sympathetic Ganglionectomy and Trunk Resection, J. Lab. & Clin. Med. **15**:1247 (Sept.) 1930.

Their observations were limited to clinical cases because the cause of chronic arthritis is still unknown and the typical disease has not yet been produced in experimental animals (Key[16]). Consequently, it is not possible to determine in experimental animals the effect of any form of therapy on this condition.

However, one of us (Key[17]) has shown that if a rectangle of the articular cartilage is removed from the patellar surface of the femur of rabbits, in a large percentage of the animals a chronic progressive

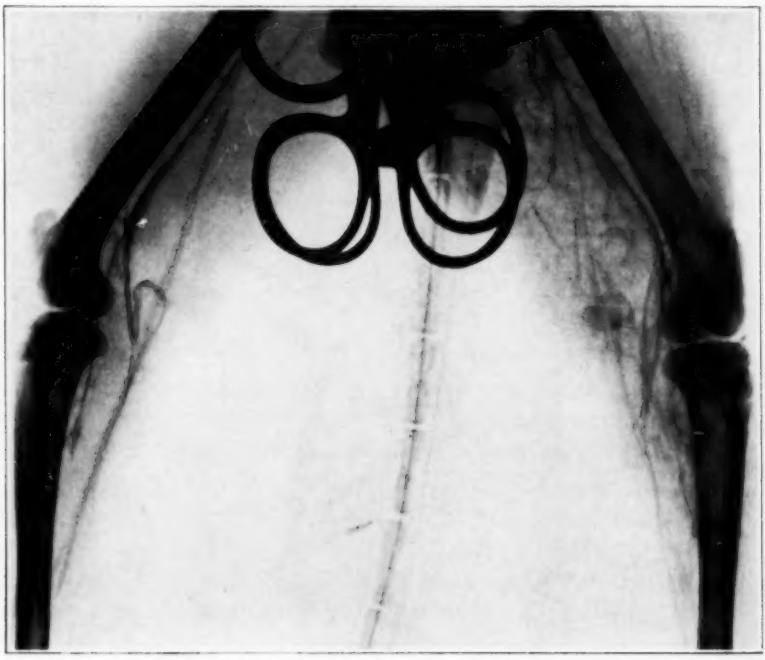


Fig. 2.—X-ray photograph of the hind limbs of a living cat taken after the injection of 1.5 cc. of 100 per cent sodium iodide into the abdominal aorta. Ten weeks previously a left lumbar sympathectomy had been done. The arterial system of the left limb is still greatly dilated as compared with that of the right.

arthritis will develop in the knee operated on. Consequently, it was decided to determine the effect of sympathectomy on this type of experimental arthritis.

16. Key, J. A.: Pathogenic Properties of Organisms Obtained from Joints in Chronic Arthritis, Proc. Soc. Exper. Biol. & Med. **26**:863, 1929.

17. Key, J. A.: Experimental Arthritis: The Changes in Joints Produced by Creating Defects in the Articular Cartilage, J. Bone & Joint Surg. **13**:725 (Oct.) 1931.

Materials and Methods.—In this series of experiments a rectangle of cartilage approximately 3 by 5 mm. was removed from the patellar surface of the femur in each knee joint of a series of thirteen cats. Either at the time of the operation on the knee or from one to two months later, left lumbar sympathectomy and splanchnotomy were performed on these animals. They were then killed at intervals of from six to twelve months after the operation on the knee, and the knee joints were studied in the gross and microscopically.

Results.—As well as we could determine by gross and microscopic examination, the cartilage healed in practically the same manner and at practically the same rate in the sympathectomized limb and in the control joint of the other leg of the same animal. In all of these animals the defect tended to heal by fibrous tissue, and in some instances partly by regeneration of the cartilage, and there was no evidence of the expected chronic arthritis developing in any of the cats such as one of us (Key) has described in rabbits after similar defects in the articular cartilage.

COMMENT

It has been demonstrated (Moore, Williams and Singleton[18]) that lumbar sympathectomy and splanchnotomy as performed by us result in a vasodilatation in the corresponding hind leg which lasts for at least ten weeks and which is sufficiently marked to be visualized in x-ray photographs of both hind legs taken after a 100 per cent solution of sodium iodide has been injected into the abdominal aorta (fig. 2). It is thus evident that the operation as performed on our animals is an adequate test as to whether or not sympathectomy influences the healing of cartilage in the extremities operated on.

We were led to perform these experiments on cartilage largely because of our interest in chronic arthritis. It has been shown by one of us (Key) that if a rectangular defect is created in the cartilage on the patellar surface of the femur in rabbits, these animals may be expected to develop a progressive chronic arthritis in the joints operated on. Much to our surprise, none of the cats operated on developed arthritis. At the present time we are not able to explain this difference in reaction between the two animals. It cannot be explained on a basis of the rabbits being more active, because the cats were all kept together in a large cage and their activity was in no way restricted. It is possible that diet may have something to do with it, as the cats were fed an almost pure meat diet while the rabbits were fed a vegetable diet, but it is probable that the joints of rabbits are merely more liable to undergo pathologic changes than are those of cats.

18. Moore, R. M.; Williams, J. H., and Singleton, A. O., Jr.: The Peripheral Course of Vasoconstrictor Fibers as Revealed by a Radiographic Method, Arch. Surg., this issue, p. 308.

We have been able to produce a similar, though less marked, arthritis in dogs by the creation of defects in the articular cartilage. Thus it is seen that dogs occupy a place midway between cats and rabbits. We expect to try out the effect of sympathectomy on rabbits and dogs in which defects have been created in the cartilage of both knees in order to determine whether or not sympathectomy has any influence on the production of the arthritis.

At present our experimental observations offer no support for, or evidence against, the use of sympathectomy in the treatment of chronic arthritis. However, in the experimental animals we could detect no difference between the joints of the sympathectomized limbs and those of the controls on the other sides of the same animals.

In our experiments on bone healing we first resected portions of the fibula and bored holes in the tibia in the legs of cats that had been subjected to abdominal sympathectomy. These experiments gave negative results. However, the fibula is such a small bone that we did not consider the negative results as of much value. Likewise, the healing of the drill holes in the tibia were not considered an adequate test as to whether or not sympathectomy might influence osteogenesis. Consequently, we were forced to perform our operations on the bone on the fore leg, as it was necessary to have an adequate control on opposite sides and the fore leg is the only place in an animal where it is possible to operate on a relatively large bone on both sides and have adequate splintage and no crippling.

Unfortunately, the sodium iodide method was not applicable for controlling the effect of sympathectomy on the blood vessels in the fore leg. The iodide is quite toxic to the nerve centers, and the animal survives its presence in the abdominal aorta only while the aorta and the vena cava are clamped above the site of the injection. It is not possible to make a simultaneous injection into both fore legs without permitting the sodium iodide to enter the central nervous system, and this causes death of the animal and vitiates the result. However, since it has been demonstrated that the operation as performed severs all of the sympathetic fibers to the fore leg (Ranson) there is no doubt but that our experiments have been adequate to produce vasodilatation in the sympathectomized limb.

Our experiments demonstrate that in normal animals with fresh fractures sympathectomy that results in prolonged dilatation of the blood vessels of the limb operated on has no influence on the healing of fresh fractures and bone defects, but this does not rule out the possibility that sympathectomy may not be of value in some cases of delayed union. However, this has yet to be demonstrated in other than clinical observations which are open to question because they are not controlled. In a case of delayed union it is rarely possible to say

whether nonunion will or will not occur. Likewise, it will be difficult to prove this point experimentally, because in experimental animals in which large defects sufficient to cause nonunion are created our observations reveal no probability that sympathectomy may stimulate osteogenesis and cause union to occur.

CONCLUSIONS

1. Sympathectomy has no influence on the healing of fresh fractures or fresh bone defects.

2. Sympathectomy has no influence on the healing of defects in articular cartilage.

RÔLE OF INFECTION IN THE PRODUCTION OF POSTOPERATIVE ADHESIONS

GEORGE P. MULLER, M.D.
AND
LEE A. RADEMAKER, M.D.
PHILADELPHIA

The occurrence of omental and intestinal adhesions after laparotomy has been a source of trouble ever since asepsis permitted the surgeon to open the peritoneum, and frequently these adhesions give rise to more acute symptoms than the condition for which the operation was done. At first adhesions were recognized only by the occurrence of intestinal obstruction, but later surgeons noted that a picture of dull, dragging pain or of partial obstruction after a laparotomy was the result of the presence of omental bands and intestinal adhesions.

Many theories have arisen as to the etiologic factors concerned in the production of adhesions, although little experimental work has been done. Every surgeon is familiar with the protective action of omentum and of fibrinous exudate in the walling off of infection or perforation. Without this protective action, the mortality resulting from many procedures would be considerably greater than it is. It is only when these adhesions form in excessive amount, fail to absorb or form in detrimental positions that they lose their beneficial properties and become a menace to health and to the success of the operation performed. Thus in many instances adhesions of omentum that successfully wall off a ruptured appendix after operation may cause symptoms and even obstruction at a later period. Moreover, the question has often arisen as to why among persons subjected to similar technics and similar operative procedures symptomatic adhesions should develop in a certain number while others are free from them.

Infection and trauma have long been conceded to be important factors in the production of adhesions, and the etiology of the early or protective adhesions seems generally accepted as being due to these factors. The cause of the hardened or detrimental adhesions is much less understood. Factors of origin, of reabsorption and of disappearance enter into the question, and make the etiology even more complicated.

From conjecture and experimental evidence two conclusions seem possible: that adhesions are primarily formed by trauma on which irrita-

From the Surgical Division (Service B) and the Laboratory of Research Surgery, University of Pennsylvania.

tion by chemicals or bacteria is superimposed, and that the further processes of absorption are by means of phagocytosis and the action of proteolytic enzymes. We have as yet no means to determine why resolution occurs in some early adhesions while others develop into hard and detrimental types, nor can we explain the adhesions occurring in the so-called "clean" cases in which aseptic technic is used, since trauma alone, unless severe enough to admit bacterial contamination, will not produce adhesions.

The mechanism of production, the morphology and the development of abdominal adhesions have been so well described by Ladwig [1] in a recent article that additional details would be almost superfluous. His study explains many of the phases of adhesions noted clinically—in the formation, resorption, late disappearance and reformation after release by operation. Thus the readiness with which early and fresh adhesions may be broken up and their readiness to hemorrhage are easily understood from his description of the early adhesion in which are found many blood vessels with little fibrous or fibroblastic material, but much fibrin, exudate and edema with fatty tissue as a network. The later firmness of adhesions is readily explained by the additional presence of collagenous and elastic fibers, which occur only in certain adhesions, while others remain in the network stage or recede. Finally, the fact that real symptoms occur at various intervals after formation of these adhesions is explained by the contraction and condensation of these fibers, but much more by the results of repeated trauma to adhesions, which causes regrowth of more and more fibrous tissue. Ladwig has demonstrated old and organizing blood clots and nests of fibroblasts in old adhesions which suggest strongly the effect of repeated strains or trauma to the adhesions. This explains, too, the tendency of symptoms of adhesion to exacerbate rather than to decrease or disappear. If the trauma is severe enough, adhesions of this type may conceivably be torn free and the symptoms disappear. According to Ladwig's work, therefore, the adhesions of protection are the adhesions of the first stage of exudate, fibrin and edema, and all further stages are of no value or are malignant in action.

Ladwig further gave basis to explanations of resorption, in the demonstration of phagocytic action and even necrosis in first stage adhesions. He expressed the belief that proteolytic or autolytic enzymes are also present to cause the resorption of the adhesions. Recurrence of adhesions may also be explained by the presence of the nests of fibroblasts in old adhesions which are stimulated by any further trauma.

Basing our views on the fact that adhesions are found in almost all cases of infection of the peritoneum, we felt that infection was the

1. Ladwig, A.: Arch. f. klin. Chir. **151**:1, 1928.

primary factor even in the so-called "clean" cases. An experiment was accordingly devised to determine the effect of infection of wounds in the production of adhesions in noncontaminated or "clean" cases.

Guinea-pigs were chosen as the experimental animals, partially because of their extremely small and thin omentum and partially because of the lack of adhesions observed during experiments of another type. Thirty guinea-pigs were used, of an average weight of 500 Gm. The abdomen was clipped, shaved and carefully sterilized. An intraperitoneal injection of sodium amytal, shown by Lacey to produce no adhesions, was given to anesthetize the animals. An incision was then made with all sterile precautions, 1 cm. to the right of the midline in the lower right quadrant. The muscles were gently dissected down to the peritoneum. Great caution was taken to prevent opening or traumatizing of the peritoneum. The muscles were gently lifted free from the peritoneum laterally for about 1 sq. cm. In the space was placed a bit of gauze 0.5 cm. square and four layers in thickness. In one series the gauze was sterile; in another it was dipped in 5 per cent tincture of iodine and moderately dried before insertion, and in the final series it was dipped into a twenty-four hour broth culture of Bacillus coli, moderately dried and put into place without coming into contact with any surrounding structures. The muscles were then closed in layers by continuous sutures of 000 chromic catgut, and the skin was closed with silk.

After operation the series with sterile gauze showed some redness of the wound with slight edema and swelling which lasted only from twenty-four to forty-eight hours, the wound then healing uneventfully. The series in which iodine was used showed a more severe reaction, but the wound did not break down or show infection; the redness and swelling increased and disappeared in a week or ten days. The last series, as is to be expected, showed infection and abscess in all but two instances. In three the gauze was completely extruded. The mean reaction consisted of an abscess about 1 cm. in diameter, the center breaking down and healing in three weeks. The most severe reaction was a large abscess about 2.5 cm. in diameter with a crater of 1 cm. This abscess did not heal in eight weeks.

The animals were killed in from eight weeks to three months. The abdomen was opened on the left side, and the abdominal wall gently rolled over to reveal whether adhesions were present. The results were as follows:

	No. of Animals	Adhesions	No Adhesions
Sterile gauze	10	0	10
Tincture of iodine	10	1	9
B. coli	10	6	4

In each instance except those in which the gauze had been extruded, it was located and found tight against the peritoneum. The adhesion produced by iodine was firm and consisted of omentum. In the final series the seminal vesicle was twice adherent to the scar and the

omentum three times, and in one experiment with a large abscess there were adhesions of the colon, several loops of the small intestine, the liver and the omentum. Of the four animals in this series in which no adhesions occurred, two had no wound abscess and two had moderate abscesses, one of which had not quite healed in three months.

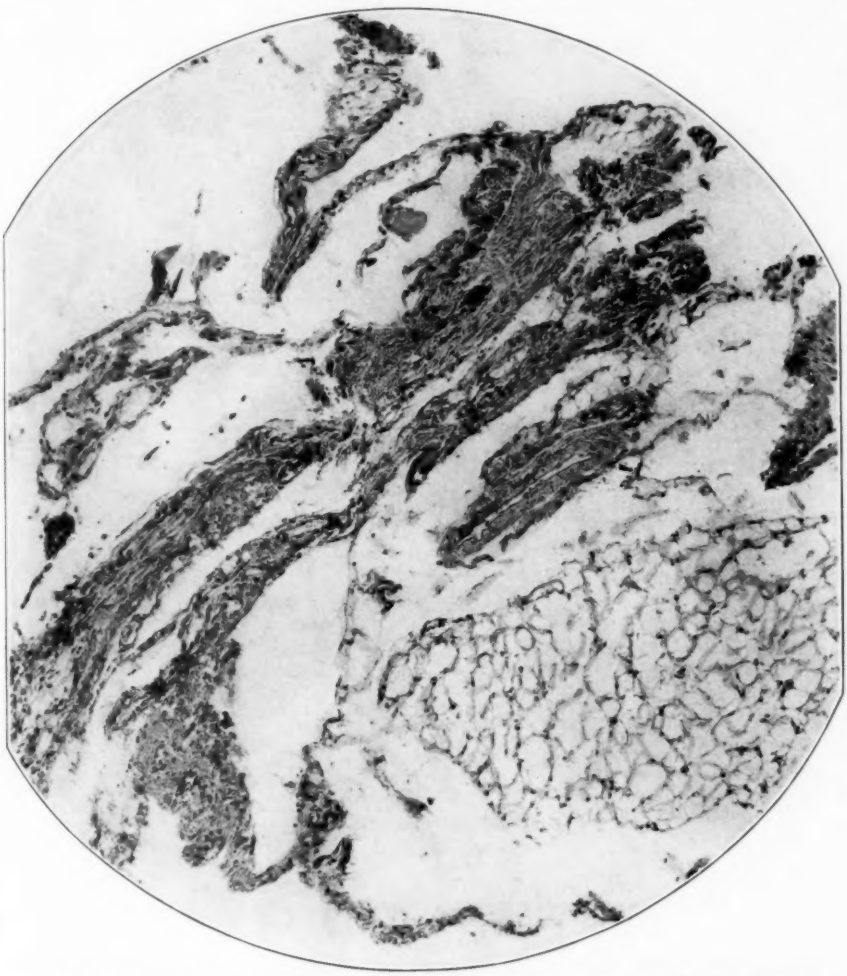


Fig. 1.—Section of human adhesion showing fibrous tissue and network of fatty tissue.

These results seemed to confirm the theory that infection is a large etiologic factor in the production of adhesions, and a survey of clinical cases was then made to trace the influence of this factor. It was obviously impossible to study the follow-up reports of all laparotomies

and determine accurately the presence or absence of adhesions. The inaccuracy of determining the presence of adhesions alone would make such a survey valueless. We therefore analyzed only those cases in which reoperation was done for symptoms caused by postoperative adhesions. Intervisceral and pelvic adhesions were ruled out and only omental adhesions to the parietal wall were chosen. A total of forty-two

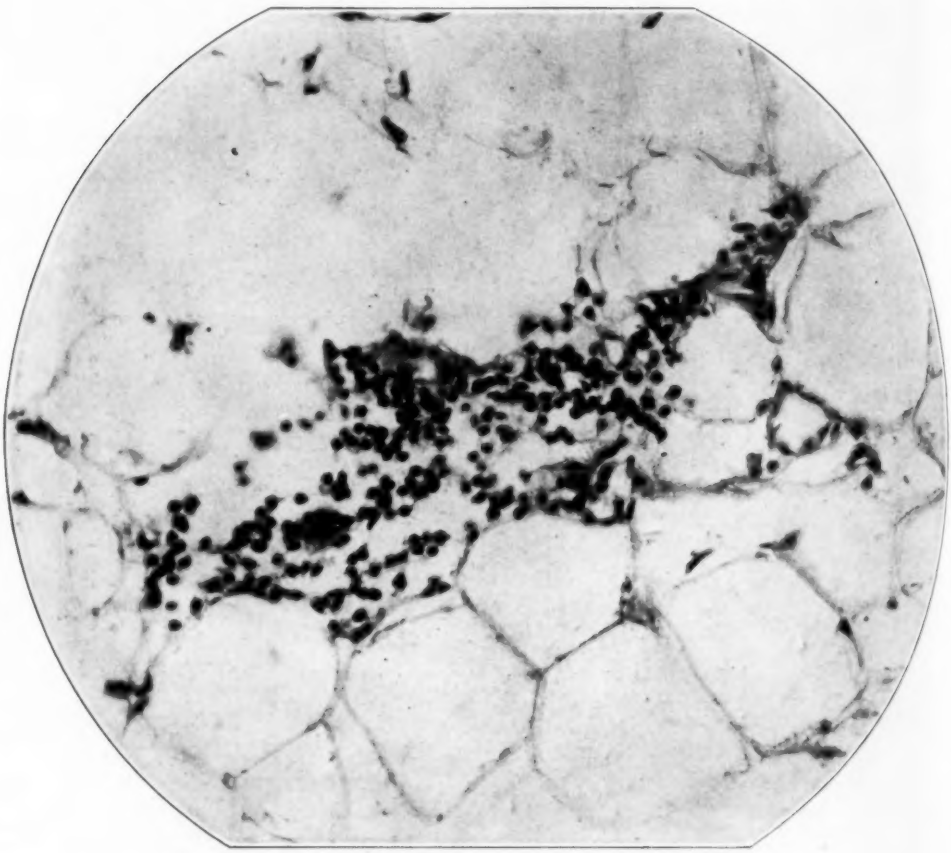


Fig. 2.—Section of human adhesion showing nest of fibroblasts.

cases were reviewed in detail. An accurate history as to infection of the wound and drainage was available in every instance from the records of the previous operation. In thirty-five of this series of forty-two patients operated on for symptoms caused by adhesions, drainage had been used, and in seven the operative procedure did not require drainage. While the use of a drainage tube does not necessarily imply the presence of infection, as in cholecystectomy for instance, the presence of a foreign body by reason of its potential infection from within the abdomen

or retrograde from skin or dressings brings these cases in the infected group. Greater interest lies in the group of seven cases in which the wound was closed without drainage, because in six of the seven the record showed postoperative infection of the wound.

Fig. 3.—Section from animal. Omental adhesion from tincture of iodine at attachment to parietal wall.

Thus in forty-two patients operated on for symptom-producing postoperative adhesions, only one had no drainage or wound infection, and of seven patients without drainage all but one had wound infections. To establish this point further morphologic and cultural studies were made in order to detect the presence of infective agents.

Fig. 4.—Section from animal. Omental adhesion from infection with B. coli, at attachment to parietal wall.

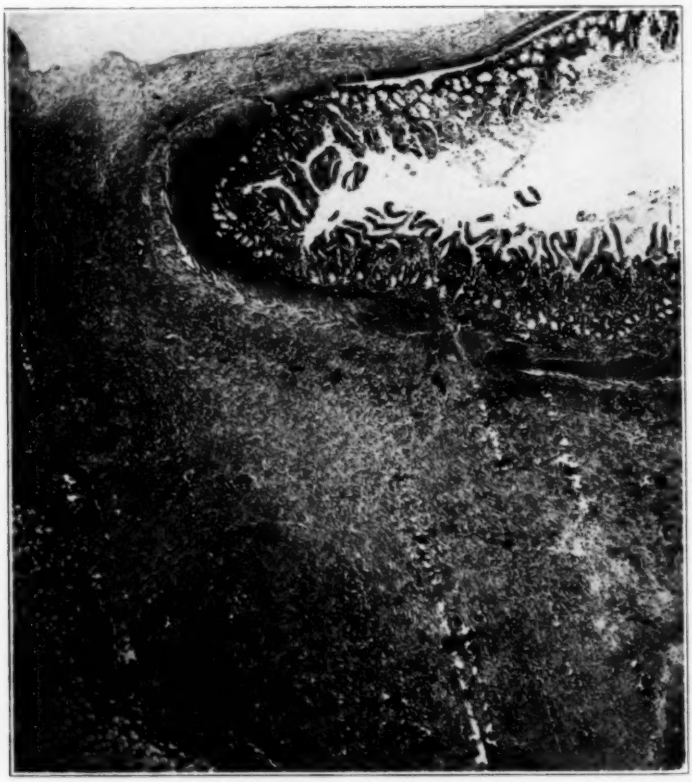


Fig. 5.—Adhesion of small intestine to abdominal wall in severe infection with large abscess.

Sections of human material were made. We could easily demonstrate the network and the collagenous fibers as illustrated in figure 1 and the nests of fibroblasts described by Ladwig (fig. 2), but careful staining and search revealed no micro-organisms. Cultures of tissue removed at operation, immediately immersed in warm saline solution and later transferred to warm bouillon have twice yielded staphylococci in recent adhesions. All other cultures have been negative. The factors of contamination are relatively large in considering absolute bacterial asepsis in the preparation of these cultures, but the positive findings in these two cases may have significance.

Comparison of the structure of the adhesions produced experimentally by iodine and of those produced by infection reveals no fundamental difference, except that the fibers of the infected adhesions go more deeply into the muscle layers of the intestines, and the direct continuity of line is lost by reason of the processes of infection in the overlying muscle layers with their fibrous tissue reaction (figs. 3 and 4). Here again, nests of fibroblasts and fibrous tissue could easily be demonstrated. No bacteria could be demonstrated in sections of animal adhesions when the animals were killed three months after operation; cultures were not made, however.

COMMENT AND CONCLUSIONS

We have presented the point of view that the primary etiologic factor in the production of postoperative adhesions is infection. An experimental study has been cited to confirm this conception. In a clinical survey we have demonstrated that intra-abdominal infection and wound infection are primary factors in causing symptomatic adhesions for which secondary operations are necessary. Finally, the morphologic structure of adhesions has been illustrated.

A NEW SURGICAL PROCEDURE FOR ACUTE PANCREATITIS

REPORT OF SIX CASES

H. H. HAYNES, M.D.
CLARKSBURG, W. VA.

CASE 1.—The first patient was a man, aged 51, who became acutely ill one day before admission to the hospital and on admission presented an acute surgical abdominal condition with distention, generalized tenderness and rigidity. He was immediately operated on under ether anesthesia. When the abdomen was opened, a large amount of brownish fluid was encountered. Fat necrosis was present, and the pancreas was enlarged and indurated.

The pancreas was drained by the transgastrocolic omental route, from the anterior surface of the pancreas, with a tube drain and a battery of cigaret drains. It drained freely for two days, but on the third day the drainage had practically ceased; under primary ether anesthesia the sinus for drainage was enlarged by blunt dissection, but satisfactory drainage was not obtained. Two days later, under local anesthesia, the gallbladder was drained. The bile was slightly darker than usual, but no stones or other lesions were found. The patient became progressively worse, and expired thirty-six hours later.

This case, as far as I am able to judge from the standpoint of early admission and general physical condition, was the best surgical risk of the series.

Apparently inadequate drainage was the chief cause of failure, although I had provided as much drainage as any textbook that I have seen recommends.

CASE 2.—The second patient was a man, aged 24, who while at dinner was suddenly seized with severe epigastric pain, accompanied by vomiting, chills and perspiration. He was admitted to the hospital the following day at 9 p. m. On admission there was slight distention of the abdomen, with tenderness and moderate rigidity in the epigastrium.

Immediate laparotomy was performed through an upper right rectus incision. There was marked fat necrosis, and the pancreas was definitely enlarged. No associated biliary lesions were found.

This was the first patient in whom the pancreas was drained by the method that will be described later in this paper. There was profuse drainage for eight days, which diminished gradually. After the first few days the patient steadily improved; he was discharged twenty-two days after the operation. He made a complete recovery and is now enjoying excellent health.

CASE 3.—The third patient was a woman, aged 32, who became ill five days before admission to the hospital. She had severe pain in the upper left quadrant, nausea and vomiting, and on entrance to the hospital was profoundly shocked, mentally confused and cyanotic. Her general condition was so grave that it seemed practically useless to submit her to an operation.

When the abdomen was opened, a large amount of serosanguineous fluid was present in the peritoneal cavity, with numerous areas of fat necrosis. The

lesser peritoneal cavity was filled with a heavy exudate, and the gastrocolic and gastrohepatic omentums were apparently on the verge of necrosis. No associated biliary lesions were found.

Drainage of the lesser cavity was established through the gastrohepatic omentum; while the posterior surface of the pancreas was being drained, the finger was introduced into the lesser peritoneal cavity by breaking through the peritoneum at the upper border of the pancreas.

Drainage was profuse; six days after operation food began to appear in the drainage, and for ten days leakage of food continued, which must have been due to sloughing of the posterior wall of the stomach. This patient made a slow recovery and was in the hospital forty-three days.

She reported to me about two months ago, in good physical condition, and stated that she "felt as well as she ever did."

CASE 4.—The fourth patient was a man, aged 40, who had been ill five days with acute pain in the upper part of the abdomen, which was not relieved by morphine. He had had a similar attack two months before presentation, which lasted two days. On admission to the hospital he was acutely ill, with moderate cyanosis and a rapid and thready pulse.

Laparotomy was immediately performed. A large amount of chocolate-colored fluid was found in the peritoneal cavity. The pancreas was swollen and discolored, with many hemorrhagic areas over the entire gland. The wall of the gallbladder was thickened, contracted and adherent to the omentum. When the gallbladder was opened, a thick, dark bile and numerous small stones were found.

The pancreas was drained from its posterior surface, and the lesser peritoneal cavity was drained by breaking through the peritoneum at the upper border of the pancreas. The gallbladder was also drained.

The pancreatic drainage was almost unbelievably profuse and showed little sign of diminishing until the third week. The patient made a satisfactory recovery after remaining in the hospital forty days.

He reported two years later; his general health was good, except for occasional attacks of moderate pain in the right hypochondriac region and tenderness in the region of the gallbladder.

CASE 5.—The fifth patient was a man, aged 50, who entered the hospital because of intense pain in the upper part of the abdomen, which began eight days before entrance to the hospital, but which had greatly increased in severity during the last seventeen hours before admittance. This patient had marked arteriosclerosis; the blood pressure was 180 systolic and 102 diastolic. There was marked tenderness in the entire right side of the abdomen, and rigidity was pronounced.

An immediate exploratory laparotomy was performed. The abdomen contained approximately a pint of a serosanguineous fluid. There was a widespread peppering of fat necrosis. The pancreas was enlarged and boggy, and was hemorrhagic throughout. There was also a postperitoneal ecchymosis along the cecum. No associated biliary lesion could be made out. The pancreas was drained by the method to be described.

There was profuse drainage in this case, and the patient made satisfactory improvement until the ninth postoperative day, when the incision opened and was immediately closed. The patient had an uneventful convalescence, and was discharged from the hospital twenty-seven days after admission.

CASE 6.—The sixth patient was a man, aged 50, who for several years had had periodic attacks of severe pain in the region of the gallbladder, with nausea and vomiting. The last attack occurred one month before admission to the hospital. His present illness began one day before admission with excruciating pain in the upper right quadrant, which was only partly relieved by repeated hypodermic injections of morphine. The patient had paraplegia of the lower extremities, which had been present since an injury to the spine in 1907.

On admission the patient was in visible distress, with pain and tenderness of the upper right quadrant and to a lesser degree of the upper left quadrant.

When the abdomen was opened, a large amount of serous fluid was found free in the abdominal cavity. The pancreas was enlarged and more firm than usual. There were a number of old, firm adhesions about the gallbladder. No gallstones were found.

The pancreas was drained by the method to be described.

He made an uneventful recovery and remained in the hospital for twenty-three days. This case was referred to me, but in my absence the operation was performed by Dr. H. E. Sloan and my associate, Dr. C. C. Greer, both of whom were familiar with the method of drainage described. Although neither of them had performed drainage by this method before, they stated that it was easily and quickly done.

After failure in my first case, when the surgical risk was apparently good, and when I had carefully followed out the well recognized transgastrocolic route of drainage with a battery of tubes and later drainage of the gallbladder, and then had lost the patient from what I believed to be inadequate drainage, I made a careful study of the anatomy in the region of the pancreas from textbooks, Edinburgh stereoscopic anatomy and cadaver, and decided that drainage from the posterior surface could be more easily and adequately obtained than from the superior or inferior surface.

With this in view I worked out the following method, which is decidedly difficult to describe and illustrate, but which is simple and easy to perform.

In this series not one case was positively diagnosed before operation, and in only three cases was pancreatitis suspected.

The symptoms usually suggested an acute pathologic condition of the upper right quadrant of the abdomen, and a right rectus incision was made in every case.

OPERATION FOR DRAINAGE FROM THE POSTERIOR SURFACE OF THE PANCREAS

A liberal right rectus incision is preferred. Before drainage is established, associated lesions should be located, and the peritoneal toilet completed. The pancreas is easily exposed by lifting the transverse colon and omentum. It is easily recognized by the characteristic pinkish color, if normal, or by the pathologic changes, if acutely diseased. The head of the pancreas rests in the curve of the duodenum (fig. 1).

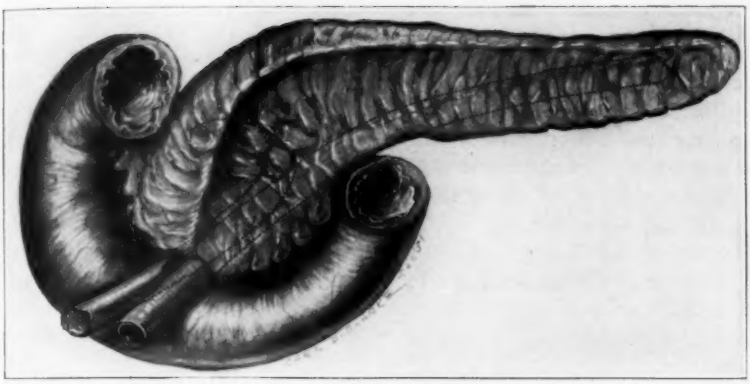


Fig. 1.—The location of the drainage tubes with relation to the pancreas and the duodenum.

Fig. 2.—The right index finger is shown freeing the posterior surface of the pancreas, preparatory to drainage, with left middle and index fingers on anterior and inferior surfaces acting as guide.

On the lower portion of the head, a little to the mesial side, there is usually a small area of peritoneum which is practically free from blood vessels. At this point the peritoneum is incised, and a blunt hemostat or dissecting scissors is introduced, and the dissection is carried down under the peritoneum to the line of cleavage between the pancreas and the duodenum. The line of cleavage is opened carefully in order not to wound the duodenum or pancreaticoduodenal vessels.

After this space has been opened sufficiently to admit the index finger, the remainder of the dissection is made entirely with the finger, and the pancreas is raised out of its normal position. With the index and middle finger of the left hand as a guide (fig. 2), it is easy to open the space immediately behind the head, body and tail of the pancreas or any part of it that the operator may

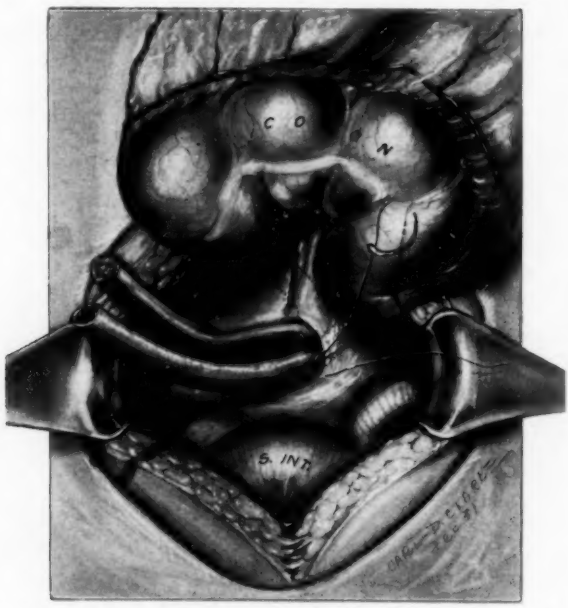


Fig. 3.—The method of draining the pancreas, showing the tube anchored to the peritoneum with no. 0 plain catgut suture.

desire. If there is a sufficient amount of inflammatory product in the lesser peritoneal cavity to necessitate drainage, it can be easily established by breaking through the peritoneum at the upper border of the pancreas. This is easily done with the finger, because bringing the pancreas forward puts the peritoneum at this point on tension. The opening is in the posterior wall of the lesser peritoneal cavity.

In two of the foregoing cases I did this and placed a drain directly into the lesser peritoneal cavity.

When making this dissection with the finger, it must be remembered that there are many important structures in this region. The most important of these are the portal vein, superior mesenteric artery and vein, pancreaticoduodenal vessels and duodenum. A safe rule is to keep the dissecting finger as close to

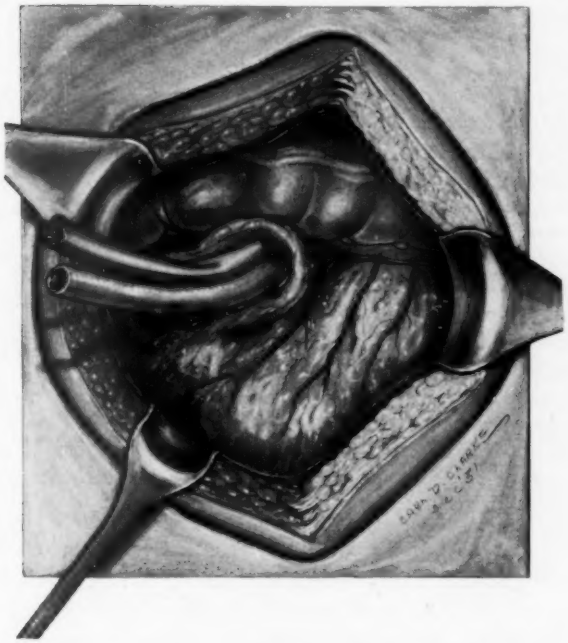


Fig. 4.—The transverse colon brought into normal position, and the omentum draped around the drainage tubes.

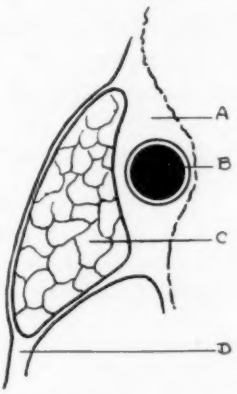


Fig. 5.—Schematic drawing of the tube drain along the posterior surface. *A* indicates retropancreatic space produced by dissection with finger; *B*, drainage tube; *C*, pancreas, and *D*, transverse mesocolon.

the posterior surface of the pancreas as possible, keeping the pancreas between the index and middle fingers of the opposite hand and bringing the pancreas forward carefully, avoiding any unnecessary disturbance of the retroperitoneal tissues.

This space should be opened thoroughly behind all the areas that are thought to be inflamed; if in doubt as to how much to open, it is better to open too much than too little; this space may be drained equally well by different methods.

The method I have used is to place a good-sized tube drain along the posterior surface, as shown in figure 1 and in the schematic drawing, figure 5, and a cigaret or Penrose tubing directly behind the head of the pancreas (fig. 1). The tube is anchored to the peritoneum with no. 0 plain catgut suture, as shown in figure 3.

The transverse colon is brought down to its normal position, and the omentum is draped carefully around the drainage tubes (fig. 4).

In closing the abdominal wall, the drainage tubes are brought out at an easy curve to prevent kinking.

Drainage following the operation varies with the severity of the case. When the drainage is profuse, after the third day I introduce a catheter through the drainage tube and irrigate with a nonirritating, sterile solution. After the fifth or sixth day the tube is removed, and irrigation is made through the sinus tract. After cleansing and sterilization, the tube is replaced.

None of the five cases drained from the posterior surface, as described, has presented any symptoms that could be attributed to lack of drainage. If drainage is the chief object of the operation, it seems that this method has decided advantages over any other method that I have been able to find. In no case has it been necessary to clamp or ligate any bleeding points about the pancreas.

The following are all the methods found in my limited library and in a review of the literature: transgastrocolic omental route, transgastrohepatic omental route, infracolic omental route, drainage through foramen of Winslow and loin drainage.

None of these methods furnish adequate drainage to the retroperitoneal space.

The main advantage of the procedure here described is that it affords:

1. Better opportunity to palpate the gland, thereby yielding a much better conception of the pathologic changes and points where drainage is most essential.
2. Better drainage (more dependent drainage).
3. Less hemorrhage.
4. Fewer postoperative adhesions.
5. Easier performance.

In my opinion this method of drainage, in the hands of competent surgeons, will materially reduce the mortality from acute pancreatitis.

MADURA FOOT

A THIRD CASE OF MONOSPOROSIS IN A NATIVE AMERICAN

MOSES GELLMAN, M.D.
Associate in Orthopedic Surgery, School of Medicine, University of Maryland
BALTIMORE
AND
JOHN A. GAMMEL, M.D.
Assistant Clinical Professor of Dermatology and Syphilology,
Western Reserve University
CLEVELAND

In some countries the deep mycoses are called surgical mycoses. Presenting, as they do at times, a surgical problem, the report of a case of Madura foot seems appropriate, as the surgeon is most likely to see such conditions in the initial stages of the disease when the diagnosis is most difficult.

The term "Madura foot" was coined by the natives of India to designate a deformity of the foot most commonly seen in the vicinity of Madura, a town situated in the southern part of Deccan, at the foot of the Eastern Ghats. When Vandyke Carter,[1] in 1860, established the fungous nature of the condition, he introduced the term "mycetoma"—tumor due to a fungus. This prominent English author in later years recognized the close resemblance of the condition to actinomycosis. During the following decades, a number of widely different fungi were thought to be the cause of mycetoma, and the subject of Madura foot became more and more confused because there was not a clear conception of the term. After the preliminary work of Brumpt[2] and Pinoy,[3] Chalmers and Archibald,[4] in 1916, gave a definition that permits a more exact differentiation from allied conditions.

From the Department of Orthopedic Surgery, School of Medicine, University of Maryland, Baltimore, and the Department of Dermatology and Syphilology of the Lakeside Hospital and of the Western Reserve University, School of Medicine, Cleveland.

1. Carter, Henry Vandyke: Tr. M. & Phys. Soc. **6**:104, 1860, quoted by Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, ed. 3, New York, William Wood & Company, 1919.

2. Brumpt, E.: Les Mycétomes, Arch. de parasitol. **10**:489, 1906.

3. Pinoy, E.: Actinomycoses et Mycétomes, Bull. Inst. Pasteur **11**:929 and 977, 1913.

4. Chalmers, A. J., and Archibald, R. G.: A Sudanese Maduromycosis, Ann. Trop. Med. **10**:169 (Sept.) 1916.

We do not wish to go too much into detail, as one of us [5] in recent years reviewed this subject elsewhere. It will be sufficient to state, then, that a mycetoma is a growth or granuloma characterized by sinus formation. White, yellow, black or red granules made up of fungous elements are found either in the discharge or embedded in the pathologic tissue.

The presence of definite granules differentiates the mycetomas from other mycoses such as pseudomycetomas and paramycetomas. Chalmers and Archibald [4] subdivided the mycetomas into: (1) actinomycoses, or those forms of mycetoma with granules composed of fine nonsegmented mycelial filaments in which usually the walls are not clearly defined from the contents and in which chlamydospores are absent, and (2) maduromycoses, or those forms of mycetoma with grains composed of large segmented mycelial filaments possessing well defined walls, and usually chlamydospores.

It is obvious that the actinomycotic type of mycetoma is nothing but an actinomycosis of the foot and should not be separated from the actinomycoses in general. It is equally obvious that maduromycoses may occur in any part of the body, just as the actinomycoses do.

As knowledge of the etiology and experimental pathology of mycetoma is in a state of constant evolution, it is not astonishing that this classification already has become somewhat obsolete. There are actinomycoses known in which grains ("sulphur granules") are absent. In fact, it is doubtful whether one is justified in still making the presence of grains composed of fungous elements the criterion by which one differentiates the deep mycoses, since Tarozzi and Barbanti [6] demonstrated that it is possible to produce experimentally the picture of mycetoma with one of the best known surface parasites, Achorion schoenleinii. In keeping with the etiologic classification of diseases in other fields of medicine, the mycologic standpoint seems the only logical one. But most fungi found in mycetoma are fungi imperfecti or hyphomycetes, the botanic position of which is rather problematic and by no means final. Therefore, the classification of Chalmers and Archibald [4] still gives the clinician a satisfactory lead in solving his mycologic problems and in classifying the mycoses.

It is evident from the preceding paragraphs that Madura foot is merely a clinical term and synonym for mycetoma of the foot. It does not imply any information as to the etiology, except as to the fungous

5. Gammel, John A.: The Etiology of Maduromycosis: With a Mycologic Report on Two New Species Observed in the United States, Arch. Dermat. & Syph. **15**:241 (March) 1927; Der Madurafuss, Zentralbl. f. Haut- u. Geschlechtskr. **29**: 393, 1929.

6. Tarozzi, G., and Barbanti, R.: Actinomicosi e Monosporosi, Atti. d. r. Accad. di sc. lett. ed arti, Modena, sez. sc., s. 3a **12**:321, 1916.

origin and the presence of granules. The maduromycoses or "true mycetomas" (Pinoy, 1913) are of greater interest than the actinomycoses on account of the variety of fungi found in this type of mycetoma. Yet the clinical and pathologic pictures produced by these organisms, belonging to three different classes of the vegetable kingdom, are quite uniform. Ten genera harbor fungi described as causes of maduromycosis: Madurella, Indiella, Glenospora, Monosporium, Torula, Allescheria, Aspergillus, Sterigmatocystis, Penicillium and Mucor. All of these molds have one common feature: In their defense against unfavorable conditions in the host or in culture they are able to form granules of various sizes, shapes and colors. These granules are composed of hyphae, spores and usually chlamydospores and are easily visible to the naked eye.

TABLE 1.—*Maduromycoses in the United States*

Author	State	Localization	Color of Grains	Causative Fungus	Where Reported
J. H. Wright.....	Mass.	Foot	Black	Unknown	Tr. A. Am. Phys. **13**: 471, 1898
Boyd and Crutchfield..	Texas	Foot	White	Allescheria boydii	Am. J. Trop. Med. **1**: 215 (July) 1921
Gammel, Miskdjian and Thatcher	Ohio	Foot	Black	Madurella americana	Arch. Dermat. & Syph. **13**: 66 (Jan.) 1926
Thompson and Ikeda..	Minn.	Foot	Black	Madurella ikedai	Arch. Surg. **16**: 764, (March) 1928
C. R. Halloran.....	N. Y.	Foot	Melanoid	Unknown	Arch. Dermat. & Syph. **16**: 611 (Nov.) 1927
Puestow.....	Wis.	Neck	Black	Aspergillus nidulans	Arch. Dermat. & Syph. **20**: 642 (Nov.) 1929
Gay and Bigelow.....	Mass.	Foot	White	Monosporium apiospermum	Am. J. Path. **6**: 325 (May) 1930
Jones and Alden.....	Ga.	Foot	White	Monosporium apiospermum	J. A. M. A. **96**: 256 (Jan. 24) 1931

It is somewhat difficult to analyze the literature on mycetoma or Madura foot observed in the United States, because the mycologic data in some of the earlier reports are inadequate. For the sake of brevity and convenience, we have tabulated those cases in which we were reasonably sure that the condition was maduromycoses. Either thick septate hyphae have been described or black granules were seen, for proved cases of actinomycoses with black grains have hitherto been unknown.

The tabulation shows, contrary to expectation, that in a tropical or subtropical disease the majority of the reports originate from the northern part of the United States, but on closer analysis it is found that most patients originally came from the South. Wright's patient might have acquired the infection in Italy; only Puestow's patient had never been south prior to the onset of the illness. The fact that all but one case have been reported during the past decade is due to

increased interest and more widespread knowledge of the disease rather than to an actual increase in the number. The last two cases reported from this country were due to Monosporium apiospermum. We shall report a third case caused by the same organism.

REPORT OF A CASE

History.—G. R., born in 1875, a colored laborer, gave a history of having had a genital sore in 1895 and smallpox in 1906. Since 1910, he had had three separate injuries to the right foot while living on a farm in Virginia, from each of which he seemed to have recovered without any visible change in the condition of the affected part.

In 1917, the right foot was crushed by a wagon in a street of Baltimore and rather severely injured. The patient thought that since that time the ankle and foot had remained swollen and tender, but though he limped, he was able to do heavy labor. Two years later, the foot became larger and more painful, and there was a discharge from numerous openings. The patient entered the Baltimore City Hospital and received, aside from local attention, antisyphilitic treatment, though the Wassermann reactions of the blood and spinal fluid were negative. In the same year he spent nine days at the University Hospital. The records (1919) indicate that there was a brawny induration about the ankle and foot on which were several whitish nodular elevations and two sinuses from which came a thin grayish discharge. The roentgen diagnosis was chronic syphilitic osteitis. In spite of the handicap of an enlarging, discharging and painful foot, the patient continued to work until March, 1926, when all of the symptoms became aggravated.

The patient was admitted from the dispensary to the orthopedic service of the University Hospital on Aug. 5, 1926.

Examination.—Physical examination gave negative results, except for the loss of weight and a low grade fever, rarely over 99.6 F. The right foot, the ankle and the lower half of the leg were swollen to about three times the normal size. The swelling was tender and brawny, though in some places it was boggy. Over the entire dorsum of the foot and about the ankle were multiple punched-out, flat-mouthed sinuses, white around the edges, which when probed were found to be fairly deep and from which a thin, grayish, purulent material discharged. No granules were ever seen, though sought for. The longitudinal arch had collapsed, and the foot was markedly abducted. There were no sinuses on the leg. Movements of flexion and extension at the ankle were retained. The toes and heel appeared to be of normal size, and they were not involved.

Laboratory examination showed that the urine was normal. The blood count showed secondary anemia without leukocytosis or eosinophilia. The Wassermann reaction was negative. Cultures from the sinuses produced stapylococci and streptococci but no fungi. A report on the biopsy specimen suggested either syphilis or tuberculosis.

The roentgenograms showed a marked deformity of the entire right foot, with collapse of the bony elements. There was considerable destruction of bone with evidence of bone formation in the nature of productive periostitis of the lower thirds of the shafts of the tibia and fibula. Obliteration of the joints with fusion of the tarsus and metatarsus was demonstrated.

Fig. 1.—Lateral view of the amputated foot.

Fig. 2.—Sagittal section of the amputated foot. Part of the osseous structure is destroyed.

While the patient was in the hospital, he was given a prolonged course of potassium iodide in large doses, without improvement. Rest in bed and boric acid dressings were of no avail. The differential diagnosis rested between syphilis, tuberculosis and mycetoma, with the latter predominating, though no "grains" were ever demonstrated, even though they were diligently sought. From the physical and roentgen appearance, it was concluded that destruction and degeneration of the foot and ankle had gone so far that restitution of function was impossible.

Fig. 3.—Roentgenogram of the right foot, lateral view.

Operation and Course.—Accordingly, on September 11, amputation of the lower part of the right leg about 6 inches (15 cm.) below the knee was performed. The patient made an uneventful recovery. He was discharged on October 13, and later was able to get about fairly well on a home-made "peg-leg."

Subsequent Course.—The patient was seen from time to time. Roentgen examinations of the stump did not reveal recurrence in the bone, and there were no evidences clinically. In May, 1928, a visit to the patient's home disclosed that he had died from "stomach trouble" two weeks previously.

Pathologic Examination.—The foot and leg were swollen and indurated, and there were many sinuses of various sizes opening through the skin. On section the sinus tracts were seen to be of labyrinthine complexity, extending through

the soft tissue and bone and communicating between many tissue spaces, which were filled with thick gray pus. All of the soft tissues as well as bone were involved in this proliferative and degenerative process, and there was marked fibrosis around the necrotic areas. It was only then that, for the first time, grains were found freely in the purulent discharge.

Histologic Examination.—The histologic examination was made by Dr. Alan R. Moritz of Lakeside Hospital. There was extensive destruction and replacement of tissues by a productive inflammatory process, which was characterized by small and large and often confluent, granulomatous lesions. The smaller

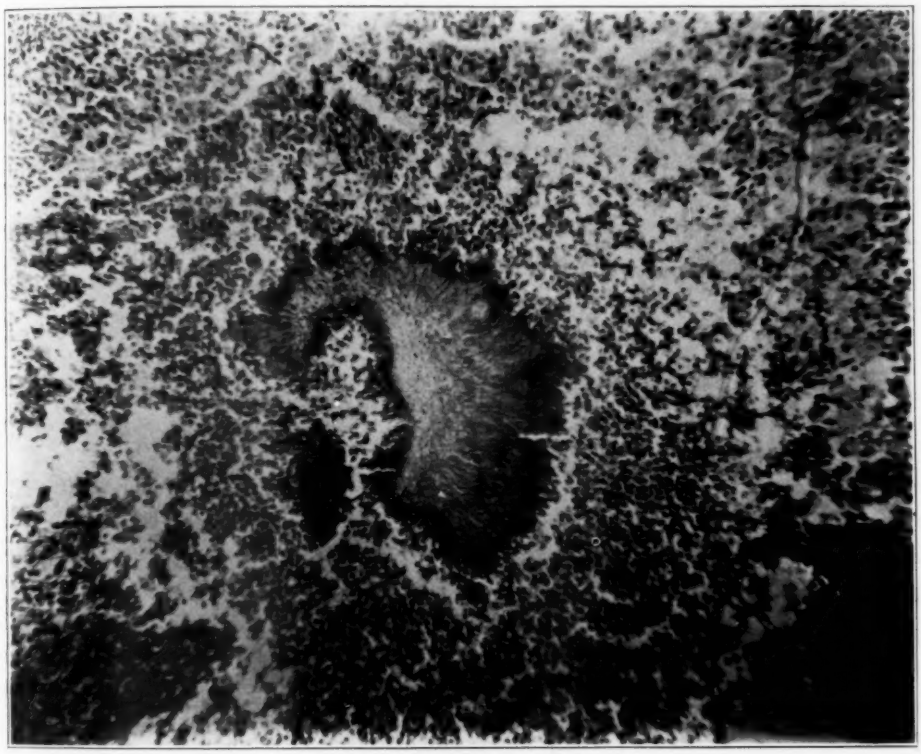


Fig. 4.—Grain in situ.

lesions consisted chiefly of focal collections of thickly disposed macrophages. These cells were round or polyhedral, approximated one another closely and had faintly acidophilic, vesicular cytoplasm. The nuclei were regular, large, round and pale-staining. Around these sharply circumscribed collections of cells there was an exudation of lymphocytes and polymorphonuclear leukocytes. These smaller granulomas were found in tissue interstices, with displacement rather than destruction of adjacent structures. The larger lesions were associated with destruction of the adjacent tissue, and intermingled with the peripheral zone of macrophages were many granulocytes, a few of which were eosinophilic. Giant cells of the foreign body type were numerous. Central necrosis was common, and the necrosis in some lesions was coagulative and in some liquefactive. The

necrotic central zones in many places were undergoing organization by polypoid masses of richly vascularized granulation tissue. Fibroblastic proliferation with resulting dense cicatrization was widespread.

In several of the granulomas, large (up to 1 mm.), irregularly outlined acidophilic granules were present. From the surfaces of these granules projected regularly disposed radial filaments, some of which were clubbed at the ends. The main body of some of the granules was comprised entirely of what appeared to be a tangled mass of acidophilic mycelium, while in others there were many

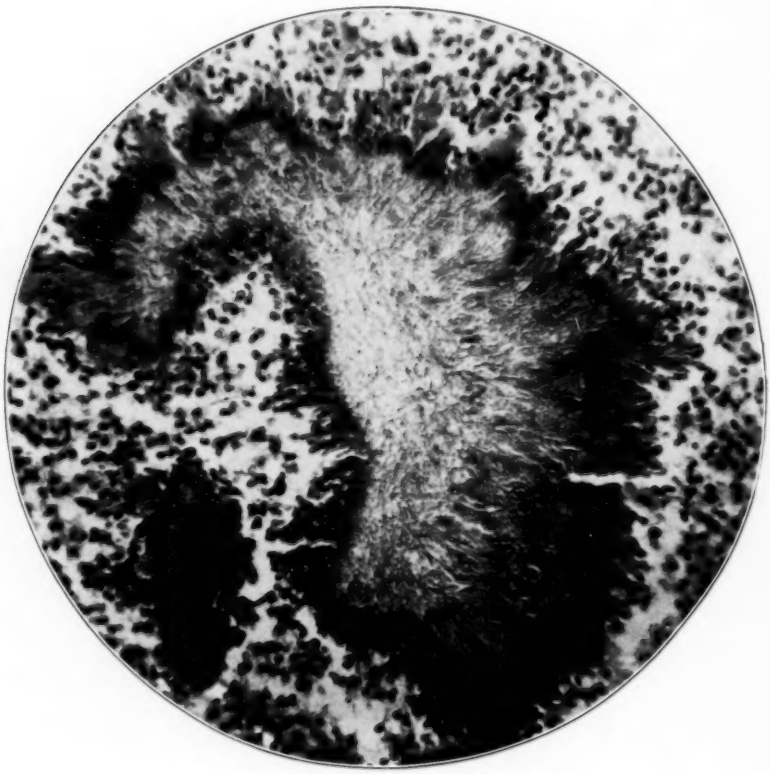


Fig. 5.—Grain in situ.

small round or ovoid, unstained, light brown spores. The spores measured about 12 microns in diameter and showed peripheral condensation. They were not confined to the granules, but were scattered diffusely, though not in large numbers, through the granulation tissue and in the central necrotic zones. Occasionally they were seen within small giant cells.

The status of mycetoma, especially the clinical side, was discussed by Thompson [7] in 1928. The case here reported is typical in all respects:

7. Thompson, H. L.: Present Status of Mycetoma, Arch. Surg. **16**:774 (March) 1928.

the history of trauma, the slow onset without a definite period of incubation, the relatively small discomfort during the first few years, the failure of iodine therapy, so efficient in some of the other mycoses, and the uncontrollable progress, necessitating eventual amputation. The rather monotonous, clinical and pathologic picture is contrasted with the multiplicity of causative organisms. Therefore the mycologic part of this study seemed to us most attractive.

When the foot was amputated in 1926, some of the granules found in the abscesses in the depth of the tissues were planted on various mediums, and the growth of a white mold was easily obtained. The thick septate mycelium established the diagnosis of maduromycosis, but an identification of the fungus was not attempted. Four years later, from 1930 to 1931, mycologic and experimental studies were carried out in the laboratories of Western Reserve University, subcultures from the original growth being used.

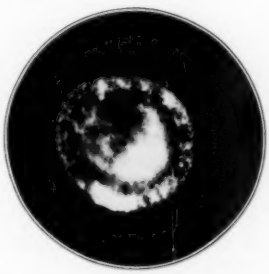


Fig. 6.—Colony of Monosporium apiospermum. One week's growth on Sabouraud's dextrose agar at room temperature.

MYCOLOGY

The fungus grows well on the usual mediums for molds. A few days after the inoculation, a snowy white tuft of fine mycelial filaments appears on the surface of the medium and spreads peripherally. On Sabouraud's dextrose or maltose agar the colonies reach a diameter of from 1.5 to 2.2 cm. after one week and about 6 cm. after three weeks' incubation at room temperature. There is marked retardation of growth in the incubator. A full-grown culture usually shows a central knob or an elevation with radiating furrows. Concentric rings in the mycelium are sometimes seen. A constant feature is a black base from which delicate, grayish, cottony, densely interwoven hyphae rise to about from 3 to 4 mm. above the surface. The growth does not push farther than from 2 to 3 mm. below the surface of the substratum. The black color of the base is due to the darkening of the spores. There does not seem to be diffusion of the pigment into the medium. On the surface of solid mediums the formation of pinhead-sized black granules

(sclerotes) is occasionally observed. Sections stained with hematoxylin and eosin fail to demonstrate any perithecia.

The modus of reproduction was studied in hanging drop cultures with Sabouraud's dextrose peptone broth, a modified Sabouraud's technic being employed. The central part of the mycelium is closely intertwined; the peripheral hyphae are hyaline and septate and branch rarely. Their diameter varies between 2.4 and 3 microns. The hyphae or lateral conidiophores, which in turn may branch again, usually terminate in a single piriform or ovoid spore from 8 to 12 microns in length and from 4 to 5.5 microns in width. Here and there, one coni-

Fig. 7.—Monosporium apiospermum. Four weeks' growth at room temperature.

diophore seems to give rise to two or three conidia. The protoplasm of the mycelial segments and spores shows everywhere small granules or droplets. Young spores are hyaline; old ones are brown. Chlamydospores are rarely seen and then only in old cultures. Gelatinized human serum is not liquefied; gelatin shows liquefaction.

The cultural and morphologic characters clearly classify the fungus as a hyphomycete belonging to the order Conidiosporales, suborder Sporophorineae. Our observations correspond in the essential features with Saccardo's [8] description of Monosporium apiospermum. Compar-

8. Saccardo, P. A.: Sylloge fungorum omnium hucusque cognitorum, 1911, vol. 22, p. 1287. Information through courtesy of Dr. John H. Barnhart, New York Botanical Garden.

ing the mycologic data in the literature on the various strains, we found considerable variations in the descriptions, which, however, prominent mycologists consider as being within physiologic limits. We hesitated at first to identify the fungus in question as Monosporium apiospermum because sometimes more than one spore is born on a conidiophore, but we found that this deviation from the original description has been

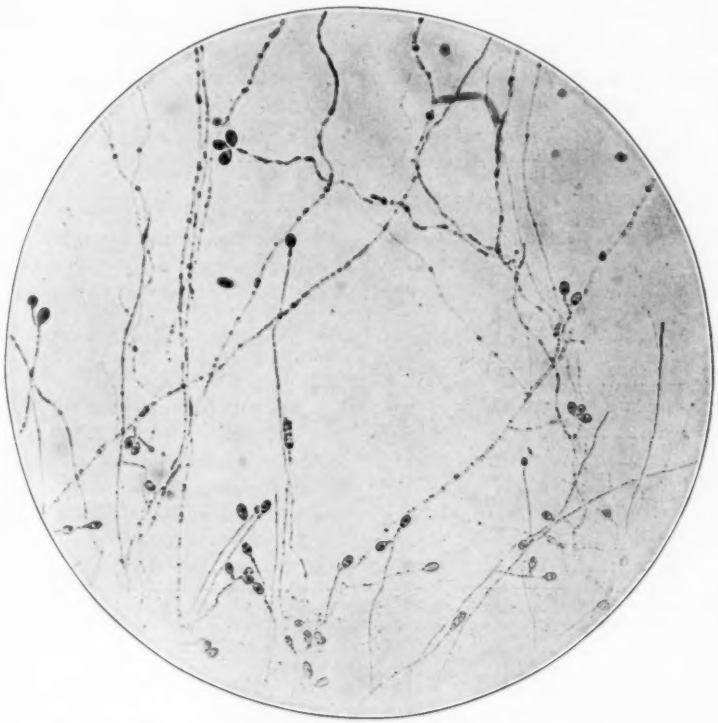


Fig. 8.—Hanging drop culture of Monosporium apiospermum.

observed by other investigators,[9] too, and Prof. Gino Pollacci [10] of the University of Padua concurred in our diagnosis.

Monosporium apiospermum, Saccardo [8] (1911) is found in the literature also as Scedosporium apiospermum (Saccardo, 1911) and as Aleurisma apiospermum (Saccardo), (Maire, 1921 [9]). It is considered by many to be identical with Scedosporium sclerotiale (seu nigricans,

9. Montpellier, J., and Gouillon: Mycétome du pied (type pied de Madura) dû à l'Aleurisma apiospermum, Bull. Soc. path. exot. **14**:285, 1921.

10. Polacci, Gino, and Nannizzi Arturo, I miceti patogeni dell'uomo e degli animali, Siena, Stab. Arti Grafiche S. Bernardino, 1923, pt. 2.

Pepere, 1914 [11]). Table 2 shows that it has been found in Europe, Africa and both Americas. It has been observed as the cause of maduromycosis more frequently than any other organism. Unfortunately, our studies, too, have failed to reveal the complete life cycle of the organism or its host.

ANIMAL EXPERIMENTATION

Suspensions of spores and hyphae from cultures were injected into the knee joints of two rabbits. After two weeks a swelling developed in both animals at the site of injection, which gradually enlarged. One animal died after two months with a tremendous swelling of the knee;

TABLE 2.—*Madura Foot Due to Monosporium Apiospermum*

Author	Country	Animal Experiments	Where Reported
Tarozzi	Italy	Positive	Atti d. Soc. ital. di. patol., set. 1909
Radaeli	Italy	Positive	Sperimentale, Arch. di biol. **65**: 383, 1911
Pepere	Italy	Positive	Sperimentale, Arch. di biol. (suppl.) **67**: 213, 1913; **68**: 531, 1914
de Magalhães	Brazil	None	Ann. da policlin. geraldo, Rio de Janeiro, Dec., 1916
Linhares	Brazil	None	Thèse de Rio de Janeiro, 1917
Montpellier and Gouilion	Algeria	None	Bull. Soc. path. exot. **14**: 285, 1921
Montpellier	Algeria	None	Bull. Soc. path. exot. **17**: 755, 1924
Anderson	Algeria	None	Arch. Inst. Pasteur de Tunis **14**: 90, 1925
Fonseca and Area Leao	Brazil	None	Compt. rend. Soc. de biol. **97**: 1347, 1927
Delamare and Gatti*	Paraguay	None	Compt. rend. Acad. d. sc. **188**: 1264, 1931
Gay and Bigelow	U. S.	Negative	Am. J. Path. **6**: 325 (May) 1930
Jones and Alden	U. S.	Negative	J. A. M. A. **96**: 236 (Jan. 24) 1931

* This organism was originally described as Indiella americana but was later identified by Paul Peña as Monosporium apiospermum (Compt. rend. Soc. de biol. **104**: 689, 1930).

crepitus could be felt easily. Unfortunately, the animal was disposed of by the attendant before autopsy could be performed. At the same time, the other animal seemed to show some improvement, there being less swelling and local heat. It was killed on the seventieth day. There were several walled-off abscesses around the knee. The synovial fluid was increased and slightly purulent. Retrocultures from bits of muscles, from the abscesses and the articular fluid gave positive results. A detailed study of the mechanism of the infection in a larger series of animals will be published later.

11. Pepere, A.: Micetoma a grani neri del piede, Sperimentale, Arch. di biol. (suppl.) **67**:213, 1913; Sul funge parasita di un micetoma a grani neri del piede (Carter) nostrana [Monosporium apiospermum, Sacc., (M. sclerotiale)] Sperimentale, Arch. di biol. **68**:531, 1914.

SUMMARY

A third case of monosporosis under the clinical picture of Madura foot of the white grain variety occurring in a native American is reported.

Mycetomas due to higher fungi rarely respond to medical treatment (iodides and compound tincture of iodine given intravenously, etc.); therefore they belong to the domain of surgery.

In cases of chronic osteomyelitis and tuberculosis or syphilis of the bone, the possibility of a mycosis should be considered.

Monosporium apiospermum injected into the knee joints of rabbits results in a purulent arthritis with periarthritic abscesses from which retrocultures are positive. This is the first instance in which experiments on animals carried out with a fungus isolated from a patient with maduromycosis in the United States yielded positive results.

418 Medical Arts Building.

The Lakeside Hospital.

VASOCONSTRICTOR FIBERS

PERIPHERAL COURSE AS REVEALED BY A ROENTGENOGRAPHIC METHOD

ROBERT M. MOORE, M.D.

J. HARRISS WILLIAMS, M.D.

AND

ALBERT O. SINGLETON, JR.

GALVESTON, TEXAS

In view of the persisting difference in opinion among surgeons as to the efficacy of "periarterial sympathectomy" as compared to sympathetic ganglionectomy, a further study of the peripheral course of the vasoconstrictor neurons has recently been made. By means of a modification of Brooks' sodium iodide technic for the roentgenographic visualization of the femoral arterial tree, quite definite results have been obtained in the laboratory animal, which seem to constitute convincing evidence as to the location of the peripheral vasconstrictor pathways to the lower extremity.

METHOD

Brooks,[1] in 1924, demonstrated the possibility of roentgenographic visualization of the femoral arterial tree in man by means of the injection of a concentrated solution of sodium iodide. In the experiments to be reported Brooks' method has been modified only in that the iodide has been injected into the abdominal aorta, with the result that both femoral trees have been visualized at the same moment. By comparing the caliber of the larger arteries in the two limbs and the degree of filling of the smaller vessels, it has been possible to judge quite satisfactorily the degree of vascular constriction in either limb relative to the other.

Adult male cats were used in these studies. Under ether or sodium amytal anesthesia a laparotomy was done, and the abdominal aorta and inferior vena cava were isolated below the renal vessels. A temporary arterial clip was applied to both cava and aorta at this level, and from 1.5 to 2 cc. of 100 per cent sodium iodide was injected into the aorta below the clip and with the needle directed toward the aortic bifurcation.

From the Department of Surgery of the Medical Branch of the University of Texas.

1. Brooks, B.: Intra-Arterial Injection of Sodium Iodid, J. A. M. A. **82**: 1016 (March 29) 1924.

Immediately following the injection, one or more roentgenographic pictures of the hind quarters were taken with the operator holding the extremities in positions as nearly symmetrical as possible. The clips were then removed from aorta and vein, allowing resumption of femoral circulations. The entrance into the general circulation of the quantity of sodium iodide required for good visualization of both femoral trees was always followed by death within a few hours.

With occasional exceptions, this method has given a surprisingly good portrayal of the arteries of the lower extremities (fig. 1). The method is of advantage because it is objective, permitting comparison as to symmetry of caliber and of filling of identical vessels in the two limbs, photographed at the same instant under one filling-pressure. The method thus becomes useful in determining the presence or absence of unilateral changes in arterial caliber following any procedure whatsoever.

The disadvantages of the method are several. Although the sodium salt is the least toxic of the more soluble inorganic iodides, a quantity sufficient for satisfactory delineation of the vessels of both hind limbs of the cat invariably proves lethal when, the picture having been taken, the clip is removed from the cava and the iodide allowed to enter the general circulation. Therefore only one determination can be made in each animal. Furthermore, the method is limited in that it does not reveal the absolute degree of constriction or dilatation in a given artery but only its caliber relative to that of the corresponding vessel of the opposite limb.

The roentgenogram must be taken as soon as possible after the iodide is injected. Otherwise the picture shows a blurring of the intervascular spaces. There are two possible explanations of this phenomenon. One is that the shadow is due to the entrance of iodide into vessels too small for individual visualization but which in their aggregate cause a partial opacity. On the other hand, it may be that the iodide diffuses through the walls of the vessels to cause a shadow in extravascular areas. Obviously, such diffusion could not occur in so short a time from the large thick-walled arteries; its occurrence would denote the presence of the iodide in thin-walled vessels. A vasodilatation lowers resistance to flow and would favor the entrance of the solution into the smaller radicles. Therefore, whether the shadow in question is due to the presence of iodide in microscopic vessels or to its diffusion from them, the shadow will appear at an earlier moment in limbs where the arterial system is dilated. Figure 1 is a print from a roentgenogram taken approximately ten seconds after sodium iodide was injected into the abdominal aorta of a normal

cat. Figure 2, picturing conditions in the same animal from twenty-five to thirty seconds after the same injection, demonstrates this blurring and loss of contrast.

The 100 per cent sodium iodide solution is evidently quite irritating. Normal animals anesthetized to a sufficient degree to submit quietly

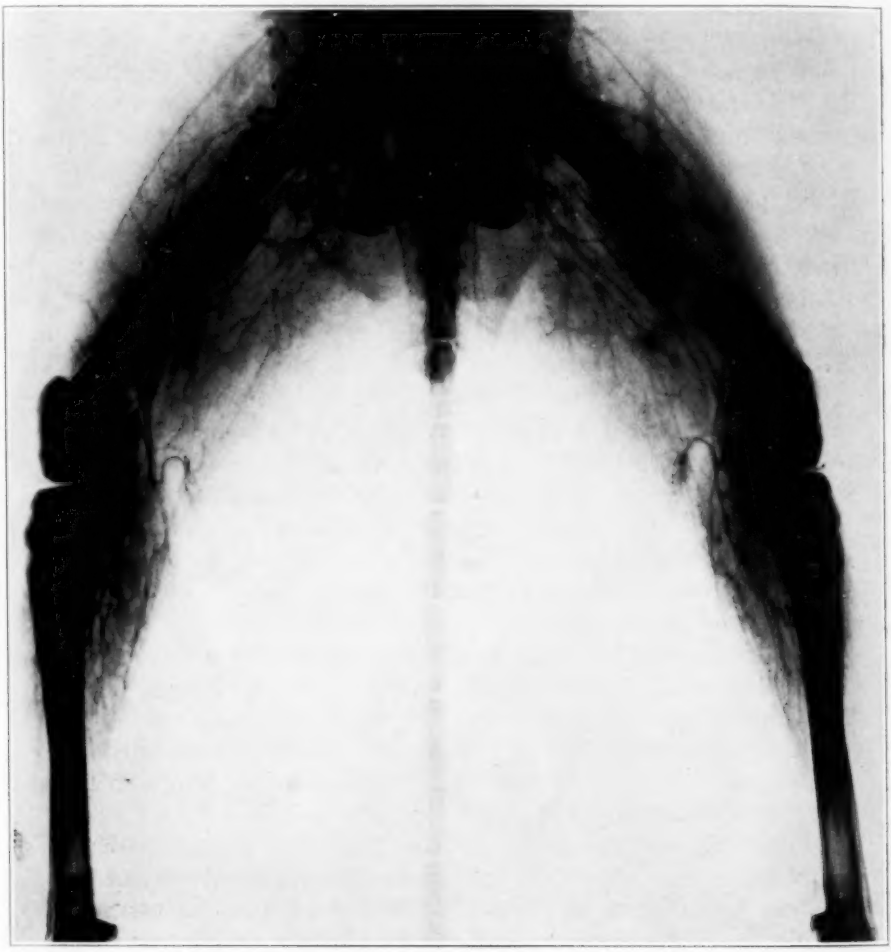


Fig. 1.—Arterial systems of lower extremities of the living cat, as shown by a roentgenogram taken ten seconds after the injection of concentrated solution of sodium iodide into the abdominal aorta.

to laparotomy invariably stir and cry out as the solution is injected into the vessels. Since a similar injection of physiologic solution of sodium chloride induces no such reaction, it must be the nature of the solution and not distention of the vessel that causes the outcry when the iodide is injected.

RESULTS

Arterial Caliber Following Sympathetic Gangliectomy.—In a number of animals a determination was made of the effect on arterial caliber of the removal of one lumbar sympathetic chain. In the cat there are five or more lumbar sympathetic ganglions. These ganglions, with the

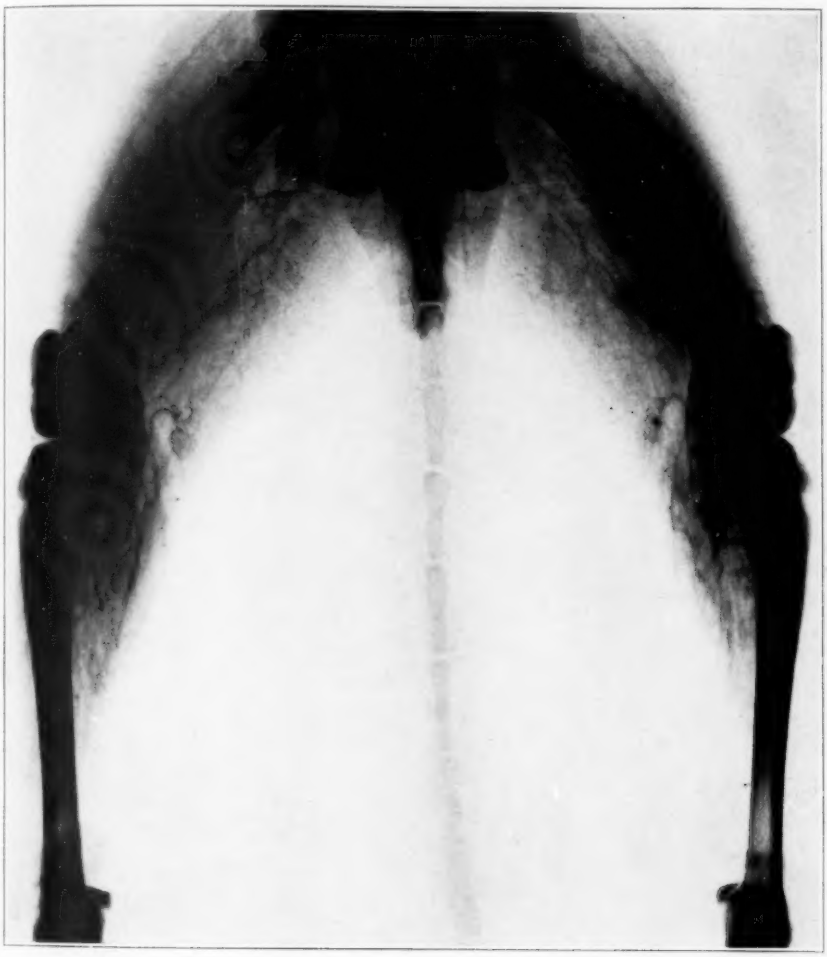


Fig. 2.—Roentgenogram of the same animal, taken fifteen seconds after figure 1. In the interim the iodide had become so distributed as to cause a blurring of the intervascular spaces.

intervening strands of fibers, were removed on one side. In order to prevent the confusing effects of reflex secretion of epinephrine, the adrenal gland of the same side was denervated by section of the major splanchnic nerve and the opposite adrenal was excised. At varying

intervals after the sympathectomy an injection of sodium iodide was given and a roentgenogram taken.

Figure 3 is a print from a roentgenogram of both legs taken immediately after resection of the left lumbar sympathetic ganglions. One sees a much greater filling of vessels on the left than on the right,

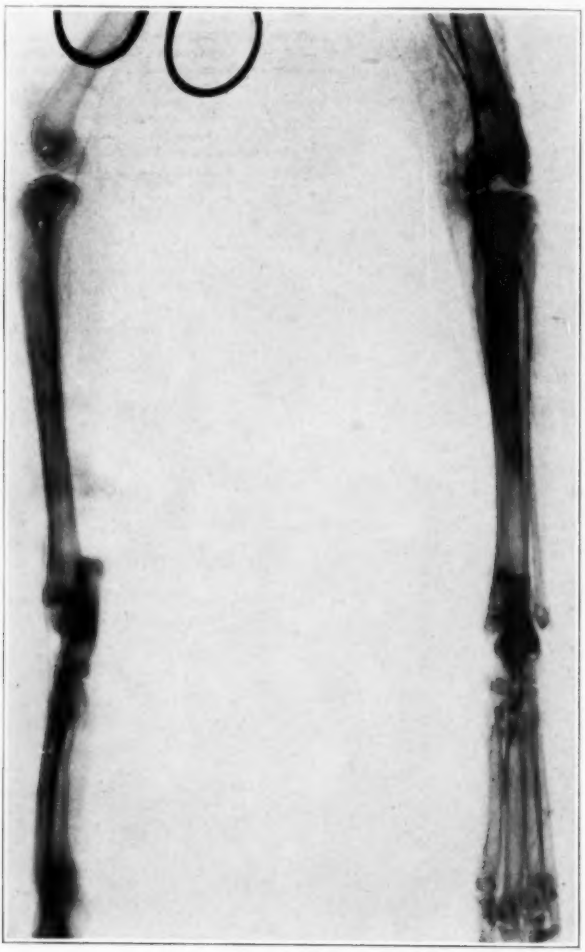


Fig. 3.—Roentgenogram of a living cat taken following the injection of iodide into the abdominal aorta immediately after left lumbar sympathectomy. The arteries of the left lower extremity are dilated relative to those of the right.

indicating a marked vasodilatation following sympathetic gangliectomy. Figure 4 shows a pronounced vasodilatation throughout the entire left extremity in an animal subjected to left lumbar sympathectomy *ten weeks* prior to the taking of the picture. Therefore, the vasodilatation

following sympathetic ganglionectomy is not a temporary phenomenon. Figure 5 was taken more than seven weeks after a lumbar sympathectomy. After the injection was made there was a delay before the roentgenogram was taken. One sees a blurring throughout the entire sympathectomized extremity. Obviously, much more iodide was present

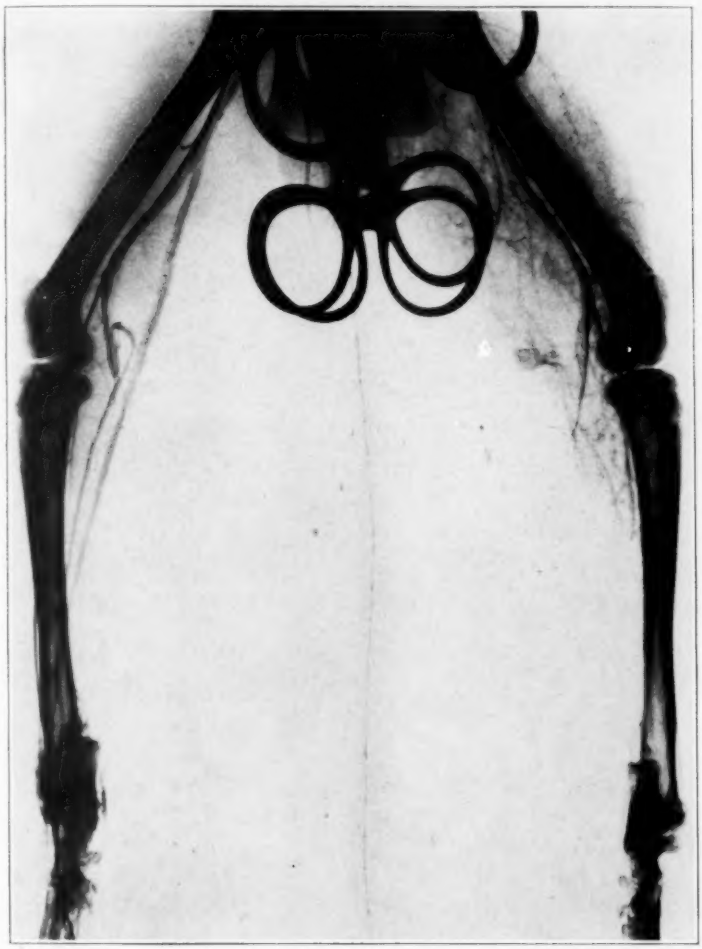


Fig. 4.—Roentgenogram following injection made ten weeks after left lumbar sympathectomy. The arteries of the left extremity are still dilated.

than was in the opposite limb. There is not a good delineation of vessels. The blurring, which regularly occurs if too much time elapses between injection and picture, must denote, as stated, the presence of iodide in microscopic radicles or its diffusion from them. In this animal (fig. 5), the blurring is much more marked on the sympa-

thectomized side, indicating a more rapid passage of the solution into the finer vessels on that side, and thus implying a loss of vasoconstriction following sympathectomy.

In the final animal of this series there was a definite increase in vascular caliber eleven weeks after sympathectomy. In our experience,

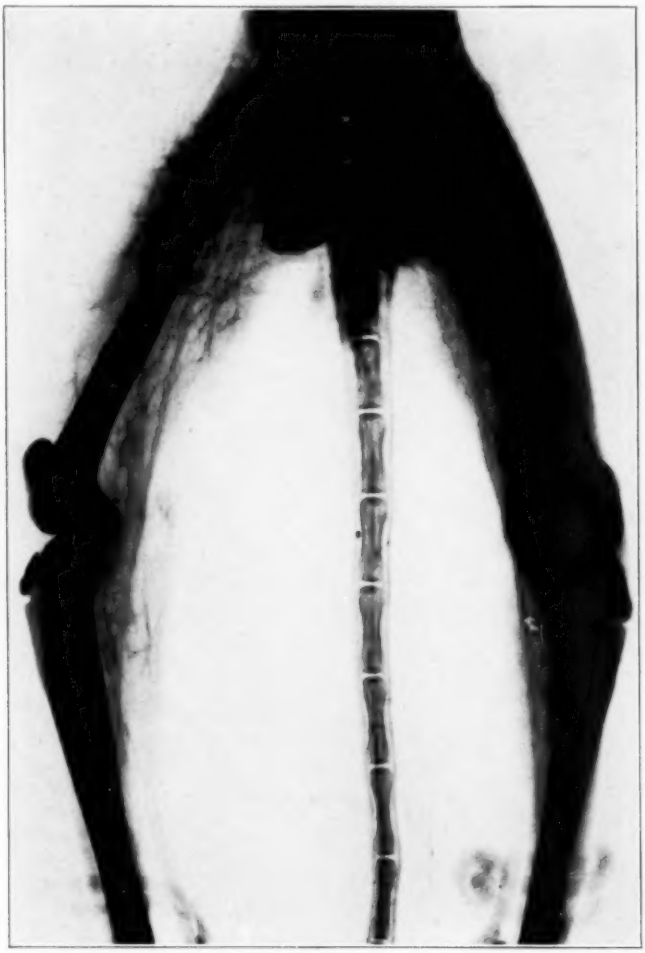


Fig. 5.—Roentgenogram following injection made seven weeks after left lumbar sympathectomy. The arteries of the left lower extremity are dilated (see text).

sympathetic ganglionectomy has always produced a vasodilatation, which has been demonstrable by the sodium iodide method.

Arterial Caliber Following the Section of Somatic Nerve Trunks.—Injections and pictures were made at varying periods of time following

the section of one or another of the peripheral nerve trunks distal to the rami communicantes. Figures 6 and 7 illustrate a result that has been of constant occurrence after section of the sciatic trunk just external to the greater sciatic foramen. One sees throughout the entire extremity, though most marked in the lateral region of the thigh, a pronounced

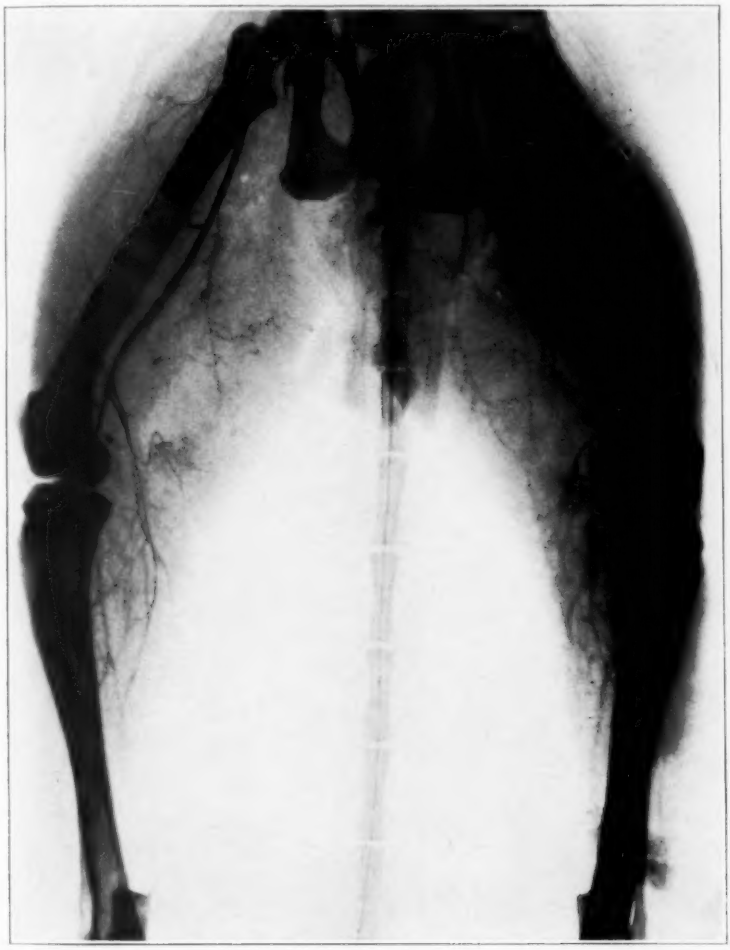


Fig. 6.—Roentgenogram showing vasodilatation in the left lower extremity following section of the left sciatic nerve.

increase in intervascular opacity as compared with the opposite limb. The area of increased opacity does not coincide with the site of the operative wound, but extends throughout the entire extremity. It is not a result of the paralysis of skeletal muscles, for it is most marked in the regions of the gluteal muscles and of the vastus lateralis, and

these muscles are not innervated by the sciatic nerve. As stated before, it must be due to the presence of the iodide in microscopic vessels or to its diffusion through their walls into extravascular areas. It seems reasonable, therefore, to consider this opacity an evidence of a vasodilatation that has permitted the iodide to enter the lumina of

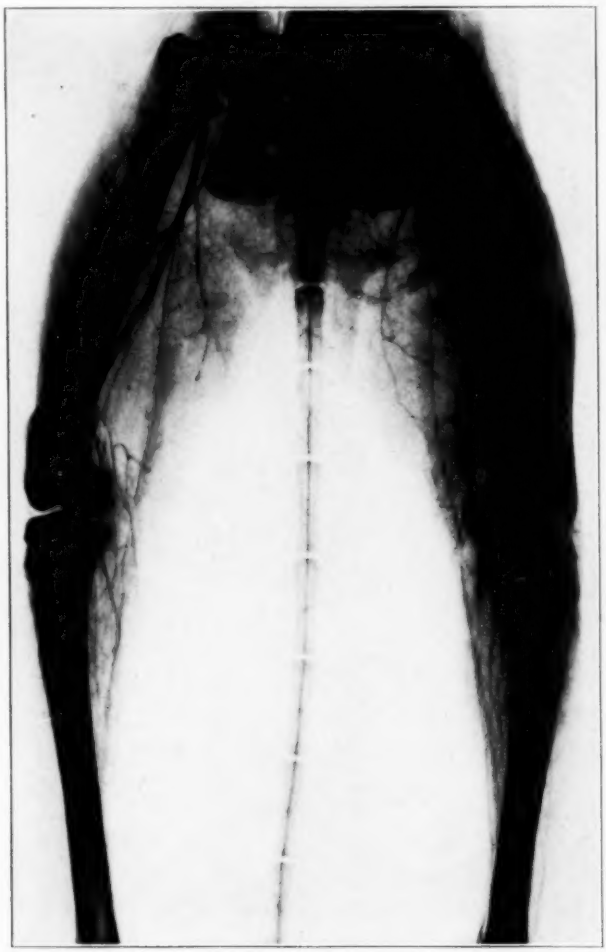


Fig. 7.—Roentgenogram showing pronounced vasodilatation in the lateral region of the left thigh following section of the left sciatic nerve.

microscopic vessels at a more rapid rate in the limb operated on than in the contralateral normal limb. The constancy of this finding has led to the conclusion that vasoconstrictor fibers are present in the sciatic nerve at the level of the sciatic foramen.

In cat 60 the femoral nerve was severed just peripheral to the inguinal ligament. Figure 8 shows the extreme unilateral dilatation of the vessels below the site of this section. Obviously, vasoconstrictor fibers were present in large number. However, this finding has been inconstant, occurring in about 50 per cent of the cases. Perhaps, since

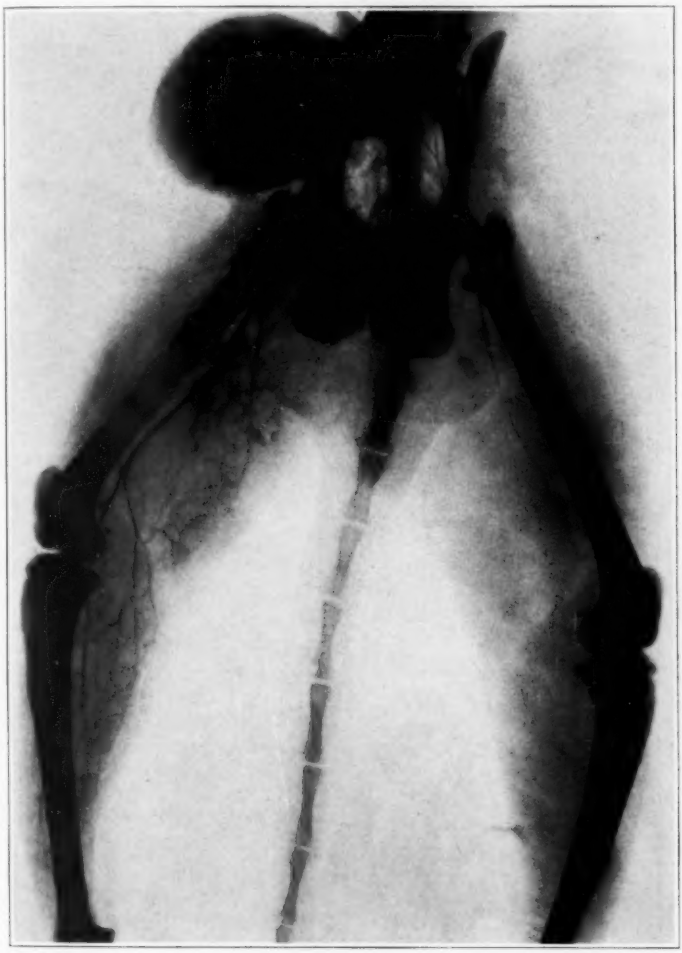


Fig. 8.—Roentgenogram showing dilatation of the right femoral arterial tree following section of the right femoral nerve.

the sciatic nerve also contains vasoconstrictor fibers, in certain instances the sciatic fibers alone may suffice to maintain vascular symmetry. Moreover, the method in use does not reveal the absolute caliber of the arteries but only the caliber relative to that of the vessels of the

opposite limb. Therefore, in those instances in which section of the femoral nerve did not result in vascular asymmetry, it is quite possible that some disturbing factor, e. g., profound anesthesia, so depressed vasoconstrictor activity throughout the entire system that section of vasoconstrictor neurons had no further effect on the size of the vessels.

Fig. 9.—Roentgenogram taken four days after right femoral "periarterial sympathectomy." No significant vasodilatation followed the operation.

Arterial Caliber Following "Periarterial Sympathectomy."—The femoral nerve of the cat lies in contact with the femoral artery. This fact forbids the use of phenol or other chemical agents as a means of detecting the presence of vasoconstrictor fibers in the periarterial region. Periarterial operations have been, therefore, mechanical, and have

included, in addition to a careful stripping of the arterial adventitia, the transverse section of all tissues of the femoral sheath except the trunk artery, the trunk vein and the femoral nerve.

In no case in our experience has this periarterial operation resulted in a vasodilatation. Figures 9, 10 and 11, showing the absence of

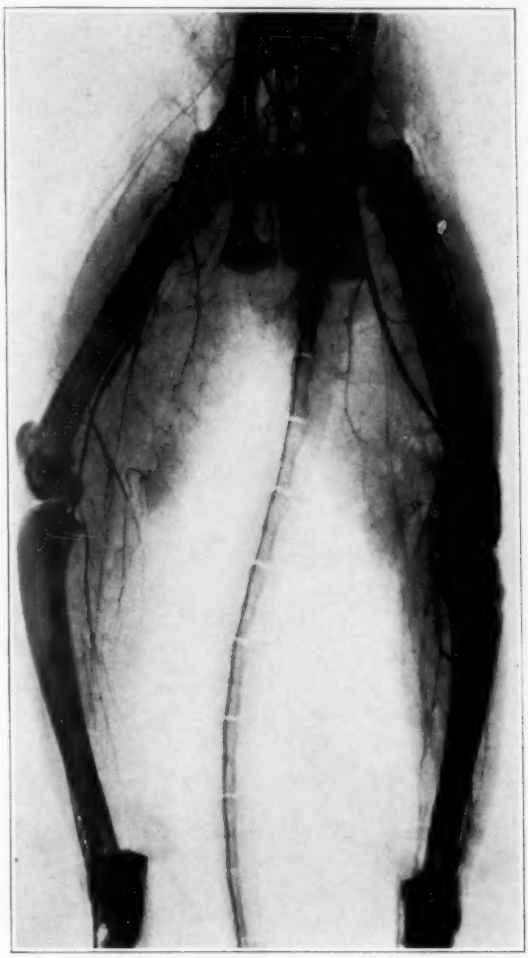


Fig. 10.—Roentgenogram taken fifteen days after right femoral "periarterial sympathectomy." No significant vasodilatation had occurred.

dilatation after four, fifteen and twenty-seven days, respectively, are representative of the series. In some cases (figs. 9 and 10) there is a slight constriction on the side operated on. (This constriction may possibly point to the presence of vasodilator fibers in the arterial sheath.) But in no instance has the periarterial operation resulted in a vasodila-

tation that could be demonstrated by this method. This series of experiments included the most satisfactory roentgenographic pictures of the entire study, and the consistently negative results would seem to be reliable proof that no great number of the vasoconstrictor fibers for the lower extremity course distally along the femoral artery.

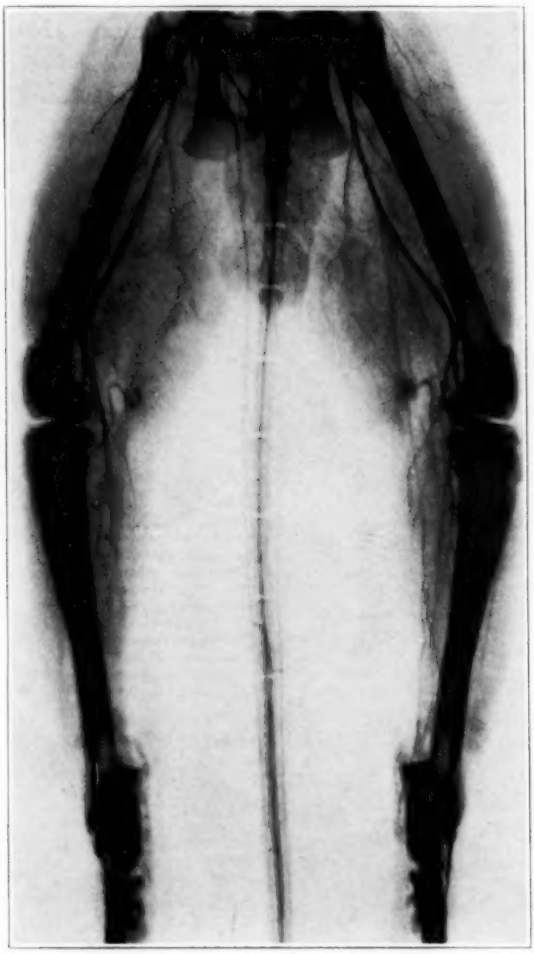


Fig. 11.—Roentgenogram showing absence of dilatation twenty-seven days after right femoral "periarterial sympathectomy."

COMMENT

It has been maintained by some, mainly on the basis of clinical changes observed following "periarterial sympathectomy," that vasoconstrictor fibers, derived supposedly from the sympathetic trunk or from the aortic plexus, extend distally along the femoral artery to play

an important part in the innervation of its smaller branches. Most anatomic findings have been to the contrary. In addition to the older writing in anatomy, recent studies by Potts [2] and by Hirsch [3] in the laboratory animal and by Blair, Duff and Bingham [4] in man have resulted in the repeated demonstration of vasoconstrictor fibers joining the peripheral arteries at irregular intervals after having been conveyed distally in the somatic nerves. Furthermore, these workers were unable to find vasoconstrictor fibers following the femoral artery for any great distance.

The roentgenographic method described in this report has revealed a pronounced vasodilatation following sympathetic gangliectomy. Although varying degrees of dilatation have occurred following the section of sciatic or femoral nerve trunks, in no instance has the periarterial operation produced any degree of dilatation demonstrable by this method. These results serve to confirm those of the authors cited, to the effect that the vasoconstrictor fibers reach the peripheral arteries by way of the somatic nerve branchings.

The literature includes at least one other attempt to study vasomotor function by a roentgenographic method. In 1930, Horton and Craig [5] reported the results of a study of arterial caliber in the lower extremities after sympathetic gangliectomy and after "periarterial sympathectomy" by means of roentgenograms taken following the injection of metallic mercury into the arteries. As the pictures were taken after death, the results cannot be interpreted in terms of nervous activity, and therefore throw no light on the issue in question.

SUMMARY

After ligation of the abdominal aorta above its bifurcation and the injection of a concentrated solution of sodium iodide just distal to the ligature, it is possible to obtain good roentgenographic portrayal of the femoral arterial systems of the living cat (fig. 1). When both lower extremities are included on one film, it is possible to compare as to symmetry of caliber and of filling the corresponding vessels of the two extremities, photographed at the same instant under one injection

2. Potts, L. W.: The Distribution of Nerves to the Arteries of the Leg, Anat. Anz. **47**:138, 1915.

3. Hirsch, L.: Ueber die Nervenversorgung der Gefässe in Hinblick auf die Probleme der periarteriellen Sympathektomie, Arch. f. klin. Chir. **137**:281, 1925.

4. Blair, D. M.; Duff, D., and Bingham, J. A.: The Anatomical Result of Peri-Arterial Sympathectomy, Brit. J. Surg. **18**:215, 1930.

5. Horton, B. T., and Craig, W. McK.: Evidence Shown in Roentgenograms of Changes in the Vascular Tree Following Experimental Sympathetic Gangliectomy, Arch. Surg. **21**:698 (Oct.) 1930.

pressure. The method thus becomes of use in determining the presence or absence of unilateral changes in arterial caliber following any desired procedure.

With this method, one can demonstrate a pronounced increase in the caliber of the arteries after sympathetic gangliectomy (fig. 3). This dilatation following resection of the proper segments of the lumbar sympathetic chain has been found persisting in animals photographed ten and eleven weeks after sympathectomy (fig. 4). No determinations have been made after longer intervals.

Section of the sciatic nerve just distal to its entrance into the extremity regularly causes a widespread vasodilatation, particularly marked in the lateral region of the thigh (figs. 6 and 7).

In approximately half of the cases, section of the femoral nerve at the root of the extremity results in a pronounced increase of the caliber of the entire femoral arterial tree (fig. 8).

In no instance has "periarterial sympathectomy" produced a vasodilatation demonstrable by this method (figs. 9, 10 and 11).

It is concluded that in the cat the constrictor neurons for the femoral arterial system are distributed to the peripheral vessels in fractions by way of the branches of the sciatic and femoral nerve trunks. No appreciable number follow the trunk artery for any considerable distance.

EXPERIMENTAL SURGERY OF THE PULMONIC VALVE

JOHN H. POWERS, M.D.
Associate Surgeon, the Mary Imogene Bassett Hospital
COOPERSTOWN, N. Y.
AND
MORRIS A. BOWIE, M.D
Instructor in Medicine, Hospital of the University of Pennsylvania
PHILADELPHIA

Two experimental procedures are included in this report: (1) the production of pulmonic stenosis in dogs and (2) the conversion of this lesion into stenosis with insufficiency by partial valvulectomy.

THE PRODUCTION OF PULMONIC STENOSIS

The method was similar to that devised for creating a chronic, sclerosing lesion of the mitral valve, which was reported in a previous paper.[1] Two distinct procedures were carried out: (*a*) electrocoagulation of the pulmonic valve and (*b*) intravenous inoculation with cultures of Streptococcus viridans.

(*a*) *Electrocoagulation of the Pulmonic Valve.*—One-half hour after the administration of morphine hypodermically, the dog was anesthetized with ether, and both sides of the thorax were shaved and cleansed with soap and water. When the animal was fully relaxed, a properly fitting rubber tube was introduced into the larynx through the trachea and attached to a Wolff bottle containing ether, which was, in turn, attached to an Erlanger mechanical respiratory apparatus. The dog was turned on its right side, and the thorax was elevated with a pad. The indifferent electrode of a portable diathermy apparatus producing a bipolar current of high frequency was placed in direct contact with the skin. The operative field was prepared with iodine and alcohol, and the dog and the operating table were draped with sterile linen. An incision was made over the left fifth rib from the angle to the sternum and was carried down through the fascia and muscle to the periosteum. The exposed rib and a portion of the costal cartilage were resected subperiosteally, and the pleura was opened. The lungs were packed off with pads of cotton moistened in warm saline solution. The sterile portion of the active electrode was then attached to the remainder of the apparatus and tested.

This study was aided by a grant from the DeLamar Mobile Research Fund.
From the Laboratory for Surgical Research of the Harvard Medical School, Boston.

1. Powers, J. H.: The Experimental Production of Mitral Stenosis, Arch. Surg. **18**:1945 (April) 1929.

The pericardium was incised medial to and parallel with the left phrenic nerve. The heart was delivered from the pericardial cavity, and a suture was placed in the apex to facilitate subsequent manipulation. A spot for the incision was chosen on the anterior surface of the right ventricle, free from coronary vessels and about 2 cm. below the root of the pulmonic artery. Control sutures were placed on each side of this area; the ends were crossed and held by the assistant. The myocardium was incised, and the insulated electrode was introduced into the cavity of the ventricle. By palpation at the junction of the pulmonic artery and the ventricular wall with the left forefinger and thumb, the operator was able both to feel and to see the location of the tip of the instrument at the pulmonic orifice. When the tip was placed in accurate approximation with the cusps of the valve, the current was applied. When the valve had been traumatized in several areas, the instrument was withdrawn and the wound in the heart was closed with silk sutures. The apex and control sutures were removed, the heart was replaced in the pericardial cavity, and the pericardium was closed with a continuous stitch of fine silk. The cotton pads were removed, the lungs were inflated, and the pleura and thoracic wall were closed in layers. If performed carefully the operation was bloodless throughout.

(*b*) *Intravenous Inoculation with Cultures of Streptococcus Viridans.*—In order to increase the reaction in the traumatized valve, each animal was inoculated twice during the early postoperative course with cultures of Streptococcus viridans. The strain of organisms utilized had been isolated from a case of rheumatic fever. Each animal was given two inoculations of from 30 to 100 cc. of a twenty-four hour broth culture of this organism, usually on the second and fourth postoperative days.

After intervals of three and ten months, two animals were operated on a second time and reinoculated.

Results.—Eight operations were performed on six dogs. The operative mortality was nil. (Similar operations on the mitral valve were followed by an immediate mortality of 22.8 per cent.[1])

Each animal was inoculated with cultures of Streptococcus viridans.

Dog 1.—A systolic murmur developed which disappeared at the end of three months. Secondary coagulation of the pulmonic valve and subsequent inoculations were repeated one month later. After three weeks a systolic murmur developed, and the blood culture was positive for approximately one month from the time of inoculation. During the subsequent five months the animal had a systolic murmur and a systolic thrill, both of which were most pronounced just to the right of the sternum in the third and fourth interspaces. Partial valvulectomy was then performed.

Dog 2.—Immediately after operation both systolic and diastolic murmurs were present. Following inoculations with cultures of Streptococcus viridans and the development of endocarditis, the diastolic murmur disappeared but the systolic murmur persisted. After an interval of two and one-half years examination of the heart disclosed a harsh, roughened first sound and a soft systolic murmur. The animal was killed, and at autopsy the pulmonic cusps were found to be slightly thickened and fibrotic.

Dog 3.—A definite systolic murmur was detected six days after operation. Two and one-half months later the murmur was present but less distinct, and it disappeared entirely in another six weeks. Twenty-seven months later no murmur was present. Postmortem examination of the heart showed two scars in the pulmonic

orifice below the insertion of the cusps which were normal. No stenosis was apparent. When the first operation was performed the tip of the instrument had not been accurately approximated to the cusps of the valve so that only the endocardium at the base of the ventricle had been traumatized.

Dog 4.—A loud systolic murmur was audible immediately after operation, and was interpreted as due to valvular damage created by the electrocautery. During the stage of acute vegetative endocarditis the murmur was less harsh, but with the

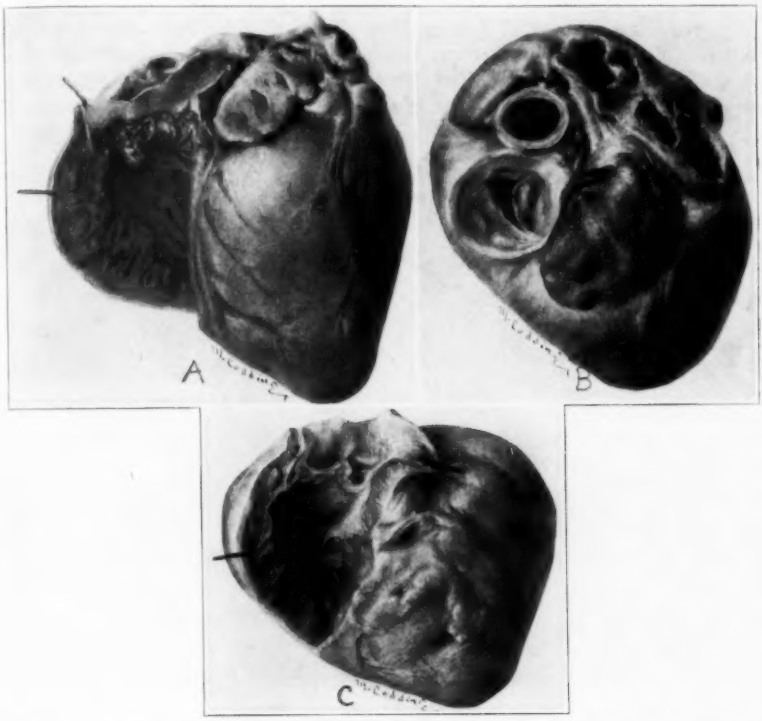


Fig. 1.—*A*, heart of dog 6. The right ventricle has been opened near the interventricular septum to expose the pulmonic valve with numerous large, warty vegetations attached to the cusps. *B*, heart of dog 1. The pulmonary artery has been cut away to expose the pulmonic valve from above. The cusps are thickened, fibrous and partially adherent to one another. The defect created by the cardiovalvulotome may be seen in the right posterior cusp. *C*, heart of dog 4. The right ventricle has been opened to expose the thickened, sclerotic posterior pulmonic cusps. The defect created by the cardiovalvulotome may be seen in the left posterior segment.

development of stenosis, it became loud and blowing. A systolic thrill was present in the pulmonic area. Partial valvulectomy was performed about six months later.

Dog 5.—Two days after the second inoculation with Streptococcus viridans (six days after operation) a soft systolic murmur was audible. A chronic discharging sinus developed at the posterior angle of the wound. The systolic murmur persisted until the animal died three and one-half months later. Autopsy disclosed

a walled-off empyema of the left pleural cavity with which the sinus communicated, diffuse fibrinous pericarditis and vegetative endocarditis of the pulmonic valve. The other cardiac valves were normal.

Dog 6.—Following operation and bacterial inoculation, a systolic murmur developed over the pulmonic area. As the acute vegetative process healed, organisms disappeared from the blood stream. With the development of stenosis, the character of the murmur changed. Three months later a long, blowing murmur was heard throughout systole. As the pulmonic obstruction increased a systolic thrill became palpable.

Secondary coagulation of the valve and reinoculations were carried out in the hope that a more marked stenosis might be produced by further trauma and a superimposed endocarditis. During the postoperative course, a very harsh systolic murmur was heard. The blood culture remained persistently positive. The dog refused food but drank much water, vomited frequently, became lethargic and emaciated, and died on the thirty-seventh day.

Fig. 2.—Roentgenograms showing the heart of dog 1, before and after the development of pulmonic stenosis.

At autopsy the pleural and pericardial cavities were remarkably free from adhesions. There were no pulmonary emboli. The pulmonic orifice was practically occluded by large, warty vegetations adherent to all three cusps (fig. 1, *A*).

Comment.—Electrocoagulation of the pulmonic valve was a less hazardous procedure than a similar operation on the mitral valve, possibly because of the proximity of the auriculoventricular node to the mitral ring. Auricular fibrillation and acute cardiac dilatation, both of which were responsible for immediate fatalities during electrocoagulation of the mitral valve,[1] did not occur in any of these experiments.

During each operation an effort was made to produce as much valvular damage as could be tolerated by the animal. Charring and puckering of the pulmonic cusps were the immediate results of the

procedure. Following intravenous inoculations with cultures of Streptococcus viridans, acute vegetative endocarditis developed on the traumatized valve. Death in one case (dog 6) was due to generalized septicemia and pulmonary occlusion caused by large, warty, fungating vegetations adherent to the margins of the valve. Four of the six animals operated on developed sufficient resistance to overcome the acute infection. As the vegetative process healed, the pulmonic cusps became thickened, fibrous and inelastic. The edges tended to adhere to one another, and chronic stenosis of the orifice was produced (fig. 1, *B*). Clinical evidence in the form of a persistent systolic murmur, accompanied occasionally by a systolic thrill in the pulmonic area, was obtained to support the diagnosis of pulmonic stenosis.

Roentgenograms of the hearts of these animals, taken at a distance of 1 meter with the tube centered over the mid-dorsal spine, showed a progressive increase in the transverse cardiac diameter, apparently due to enlargement of the right side (fig. 2).

Studies of the blood and observations of the red blood cell count, the hemoglobin and the hematocrit value after the development of pulmonic stenosis showed no significant alterations from similar determinations made before operation.

The results may be summarized as follows: One animal died from septicemia and pulmonic occlusion by vegetative thrombi. One animal died because of chronic empyema, pericarditis and acute vegetative endocarditis. In one case, clinical evidence of pulmonic stenosis disappeared at the end of three months and when the animal was killed twenty-seven months later the pulmonic valve was normal. (The tip of the electrode had not been actually approximated to the valve at operation, and consequently the cusps had not been traumatized.) In the remaining three animals clinical and pathologic evidence of pulmonic stenosis developed. Two of them were subsequently operated on again, and the stenosis was converted into stenosis with insufficiency.

None of the valves other than the pulmonary, which had been traumatized by the operative procedure, showed evidence of acute or chronic endocarditis.

CONVERSION OF PULMONIC STENOSIS INTO STENOSIS WITH INSUFFICIENCY BY PARTIAL VALVULECTOMY

Two dogs with well marked stenosis of the pulmonic valve, created by the method already described, were utilized for these experiments. Partial valvulectomy was performed with a cardiovalvulotome [2] similar

2. Dr. E. C. Cutler contributed this instrument, which was first used in some experimental studies on the surgical treatment of mitral stenosis. Beck, C. S., and Cutler, E. C.: A Cardiovalvulotome, J. Exper. Med. **40**:375 (Sept.) 1924.

to that devised by Beck and Cutler but carrying a shaft of smaller diameter.

Partial Valvulectomy.—The position of the dog on the table and the anesthesia were similar to those employed in the first series of experiments.

The heart was reexposed through the healed scar of the previous incision in the left thoracic wall. Adhesions between the pleura and the lungs or between the lungs and the pericardium were divided by sharp dissection whenever necessary. The pericardium was incised and freed from the anterior wall of the right ventricle where it was adherent at the site of the old myocardial scar. The heart was partially rotated and displaced from its pericardial bed.

Control sutures were placed; the myocardium was incised, and the cardiovalvulotome was introduced into the cavity of the right ventricle. By palpation of the pulmonic ring, at the junction of the heart and pulmonary artery, a scarred segment of the obstructing valve was engaged between the jaws of the instrument, excised and withdrawn from the circulation.

The myocardial wound was sutured, the heart was replaced in the pericardial cavity, and the pericardium, pleura and thoracic wall were closed in layers with silk.

Results.—Partial resection of the stenosed pulmonic valve was well tolerated by each dog.

Dog 1.—This was an animal with experimental pulmonic stenosis produced by the method described in the first half of this paper and recorded in the previous protocols. Partial valvulectomy was performed, and several tiny bits of scarred valve were excised. The systolic thrill disappeared, and a soft diastolic murmur was audible immediately after the operation. The systolic murmur was unchanged. One month later the presence of adventitious sounds in diastole was questionable, but the second sound was indistinct in the pulmonic area. Examination of the heart gave essentially the same results during the following twenty months. The dog was killed at the end of this period. At autopsy multiple adhesions were found between the pleura and the pericardium. (The animal had had three operations on the heart.) There were several dense scars in the pulmonic ring. The cusps of the valve were thickened, fibrous and sclerotic. The edges tended to adhere to one another at the junction of the cusps, and on the posterolateral margin of the valve was seen the defect created by the cardiovalvulotome (fig. 1, *B*).

Dog 4.—This was an animal with experimental pulmonic stenosis and a systolic murmur and thrill in the pulmonic area (see previous protocol). Several attempts with the cardiovalvulotome were made before a scarred segment of the valve was finally engaged between the jaws of the instrument and excised. The systolic thrill largely disappeared, and a questionable diastolic murmur was audible after the operation. Subsequently a long, harsh systolic murmur was always heard but no second sound could be distinguished.

The animal was killed after twenty months. The posterior and lateral cusps of the pulmonic valve were densely scarred and thickened. The anterior cusp was normal. In the posterior segment was found the defect created by the cardiovalvulotome (fig. 1, *C*).

Comment.—Both of these dogs were in good health throughout the postoperative period. No peripheral edema, demonstrable ascites or other evidences of cardiac decompensation were apparent at any time.

These results are in marked contrast to those that followed partial resection of experimental stenosis of the mitral valve in which the immediate mortality was 80 per cent and the final postoperative mortality was 100 per cent.[3]

Because of its comparatively superficial position, the pulmonic valve is relatively accessible to surgical attack. The localization of instruments within the pulmonic orifice may be assisted by both the hand and the eye. With these facts in mind, supported by the increasing tendency of surgery to encroach on the domain of the heart and accompanied by the realization that this organ will tolerate hitherto unsuspected operative manipulation, one may hope that eventually certain selected patients with congenital pulmonic stenosis will be relieved by surgical treatment.

The application of such treatment should be limited to the group of cases described by Abbott in which "the stenosis is usually valvular due to a foetal endocarditis setting in in later embryonic life after the cardiac septa have closed."

The difficulties of making such a clinical diagnosis are great, and the group of cases uncomplicated by other congenital cardiac abnormalities is small. Furthermore, a heart laboring under the embarrassment of an impaired cardiac or circulatory mechanism does not tolerate operative manipulation with the same complaisance as does the normal heart. And lastly, the patient with cardiac disease, either congenital or acquired, will submit to operation only as a last resort. Nevertheless, with improvement in diagnostic facilities and operative technic, surgical invasion of the field of congenital heart disease is not beyond the realm of possibility.

SUMMARY

Electrocoagulation of the pulmonic valve was performed on six dogs and followed by intravenous inoculation with cultures of Streptococcus viridans. Acute vegetative endocarditis developed on the traumatized valve. As these lesions healed, the cusps of the valve became thickened, fibrous and inelastic; the edges tended to adhere to one another, and the end-result was actual stenosis of the pulmonic orifice.

Two of these animals with experimental pulmonic stenosis were subjected to partial resection of the stenosed valve. The operation was well tolerated, and the animals lived for twenty months without evidence of cardiac decompensation.

The suggestion is made that the condition, in certain selected patients with congenital pulmonic stenosis, may be amenable to surgical treatment.

3. Powers, J. H.: The Surgical Treatment of Mitral Stenosis: An Experimental Study, Arch. Surg. **25**:555 (Sept.) 1932.

LOSS OF PROTEIN FROM THE BLOOD STREAM

EFFECTS OF THE INJECTION OF SOLUTION OF PITUITARY AND OF EPINEPHRINE

ALFRED BLALOCK, M.D.

HARWELL WILSON, M.D.

B. M. WEINSTEIN, M.D.

AND

J. W. BEARD, M.D.

NASHVILLE, TENN.

In previous studies,[1] the composition of the blood with particular reference to the protein content has been determined in experiments in which a decline in blood pressure produced by a variety of means was accompanied by the introduction of fluids. The fluids were injected intravenously in most of the experiments, and they included those frequently used in treating shock. In one group of studies,[1b] an unexplained decline in blood pressure occurred. This drop appeared either before or shortly following the beginning of the introduction of fluid intravenously into normal anesthetized dogs. Usually the arterial pressure remained depressed for only a short time and then returned to the previous control level. The decline in blood pressure occurred in a few of the experiments in which solutions of salt or of dextrose were used, and in most of those in which an unpurified solution of acacia was injected. In all of the experiments in which the blood pressure declined, the introduction of the fluid was accompanied by a decrease in the

From the Department of Surgery of Vanderbilt University.

1. Beard, J. W., and Blalock, Alfred: Intravenous Injections. A Study of the Composition of the Blood During Continuous Trauma to the Intestines When no Fluid Is Injected and When Fluid Is Injected Continuously, J. Clin. Investigation **11**:249 (March) 1932. Blalock, Alfred; Beard, J. W., and Thuss, Charles: Intravenous Injections. A Study of the Effects on the Composition of the Blood of the Injection of Various Fluids into Dogs with Normal and with Low Blood Pressures, J. Clin. Investigation **11**:267 (March) 1932. Beard, J. W.; Wilson, H.; Weinstein, B. M., and Blalock, A: A Study of the Effects of Hemorrhage, Trauma, Histamine and Spinal Anesthesia on the Composition of the Blood When no Fluids Are Injected and When Fluids Are Introduced Intravenously, J. Clin. Investigation **11**:291 (March) 1932. Blalock, Alfred, and Beard, J. W.: The Effects on the Composition of the Blood of the Subcutaneous Injection of Normal Salt Solution into Normal Dogs and into Dogs Subjected to Intestinal Trauma, Graded Hemorrhages and Histamine Injection, J. Clin. Investigation **11**:311 (March) 1932.

absolute amount of plasma protein. In other experiments,[1c] a decline in blood pressure was produced by the subcutaneous injection of histamine. The introduction of fluids into these animals was accompanied by a decrease in the absolute amount of plasma protein. That a decline in blood pressure per se is not the sole factor responsible for the loss of protein was shown in additional experiments [1c] in which the effects of hemorrhage and the introduction of fluids were studied. The decline in blood pressure in these experiments was not accompanied by loss of protein, except for that removed in the blood. When a drop in blood pressure was produced by the injection of procaine hydrochloride into the spinal canal, the loss of protein was not great.

The present experiments were undertaken in order to determine whether or not the loss of protein that was found in the experiments in which the unexplained declines in pressure appeared and in those in which histamine was injected could be prevented by the injection of solution of pituitary and of epinephrine. Concerning the actions of these drugs Krogh [2] stated:

> A minimal dose of adrenalin, injected into the blood or added to a perfusion fluid, normally diminishes the flow of blood to the organs studied, and such an effect is without doubt brought about by constriction of arterioles. Pituitrine, on the other hand, appears to have no effect in minute dose on the rate of inflow of blood, but a distinct effect on the blood color, brought about by constriction of the skin capillaries and venules.

METHODS

Dogs were used in all experiments. Morphine sulphate was employed as the narcotic. The studies included determinations of the blood pressure, hemoglobin and hematocrit readings and of the content of the blood serum in total protein, albumin and globulin. In the control studies, the blood volume was also determined. In subsequent studies, alterations in the blood volume were calculated from changes in the hemoglobin and hematocrit readings. In some of the experiments, the decline in blood pressure was produced by the introduction of from 6 to 10 cc. of 6 per cent unpurified acacia solution into the external jugular vein. In several instances the replacement of the blood that was removed for the control studies was associated with a decline in the blood pressure. In the remaining experiments, the decline in blood pressure was produced and maintained by the repeated subcutaneous injection of histamine. Simultaneously with the beginning of the decline in blood pressure, physiologic solution of sodium chloride was introduced intravenously at the rate of 10 cc. per kilogram of body weight per hour, and this was continued for four hours. The drugs were administered in three different ways. In some experiments, the solution of pituitary or epinephrine was placed in the salt solution that was injected intravenously. In other instances the drug was introduced intravenously in fairly large amounts during the early part of the experiments without diluting it with salt solution. In the remaining experiments, the administration was by the subcutaneous route. The total quantities of solution of pituitary and of epinephrine that were given in the various experiments varied

2. Krogh, A.: The Anatomy and Physiology of the Capillaries, New Haven, Conn., Yale University Press, 1929.

TABLE 1.—*Effects of the Intravenous Injection of Physiologic Solution of Sodium Chloride Containing Solution of Pituitary in the Presence of an Unexplained Decline in Blood Pressure*

Experiment	Time from Beginning	Amount of Fluid Given, Cc.	Pituitary Solution, Cc.	Total Protein		Albumin		Globulin		Blood Volume, Cc.			Hematocrit	Hemoglobin	Mean Blood Pressure, Mm. Hg
				Serum, per Cent	Entire, Gm.	Serum, per Cent	Entire, Gm.	Serum, per Cent	Entire, Gm.	Red Blood Cells	Plasma	Whole			
T 135	Control	0	...	6.60	69.6	2.71	28.6	3.89	41.0	(642)	(1,054)	(1,696)	37.9	88.8	120
16.3 Kg.	1 hr.	163	...	6.40	45.5	2.50	17.8	3.90	27.7	670	712	1,382	48.5	109.0	58
	2 hr. 30 min.	407	...	5.47	49.5	2.28	20.6	3.19	28.9	682	905	1,587	43.0	94.9	94
	4 hr.	652	1.6	5.34	51.7	2.21	21.5	3.13	30.2	695	970	1,665	41.8	90.5	74
	5 hr. 30 min.	...	...	5.78	51.2	2.42	21.4	3.36	29.8	699	886	1,585	44.1	95.0	74
	7 hr.	...	...	5.96	54.2	2.45	22.3	3.51	31.9	728	910	1,638	44.5	92.0	75
	Injected blood	...	...	6.98	....	3.50	....	3.48	....	...	...	.....	33.4	71.0	
T 136	Control	0	...	6.14	59.0	3.63	34.8	2.52	24.2	(440)	(960)	(1,400)	31.5	71.8	96
14.4 Kg.	1 hr.	144	...	6.37	27.2	3.39	14.5	2.98	12.7	470	428	898	52.3	111.9	50
	2 hr. 30 min.	360	...	5.61	25.7	2.88	13.2	2.63	12.5	480	458	938	51.2	107.1	70
	4 hr.	576	1.4	5.30	27.2	2.81	14.4	2.49	12.8	491	514	1,005	49.0	100.0	70
	4 hr. 50 min.	...	...	5.62	28.1	2.79	14.0	2.83	14.2	502	500	1,002	50.2	101.0	22
	Injected blood	...	...	5.70	....	2.39	....	3.31	....	...	...	.....	42.5	93.2	
T 137	Control	0	...	6.50	76.7	2.70	31.8	3.80	44.9	(775)	(1,180)	(1,955)	39.7	92.0	106
19.6 Kg.	1 hr.	196	...	6.01	61.0	2.39	24.2	3.62	36.8	795	1,015	1,810	44.0	99.3	108
	2 hr. 30 min.	490	...	5.88	65.2	2.36	26.3	3.52	38.9	780	1,110	1,890	41.3	95.1	122
	4 hr.	784	2.0	5.61	69.0	2.31	28.4	3.30	40.6	780	1,230	2,010	38.9	89.3	126
	5 hr. 30 min.	...	...	6.24	67.0	2.56	27.5	3.68	39.5	840	1,075	1,915	43.9	93.8	119
	7 hr.	...	...	6.19	68.1	2.56	28.2	3.63	39.9	880	1,100	1,980	44.4	90.9	114
	Injected blood	...	...	4.84	....	2.28	....	2.56	....	...	...	.....	19.9	45.4	

Protocols.—T 135: Decline in pressure was produced by giving 10 cc. of acacia.
T 136: Decline in pressure followed replacement of blood that was removed for control determinations.
T 137: Immediately after the blood that had been withdrawn for the control determinations was replaced, the blood pressure declined to a mean of 48 mm. of mercury and remained at that level for a few minutes.

TABLE 2.—*Effects of the Intravenous Injection of Physiologic Solution of Sodium Chloride Containing Epinephrine in the Presence of an Unexplained Decline in Blood Pressure*

Experiment	Time from Beginning	Amount of Fluid Given, Cc.	Epinephrine, Cc.	Total Protein		Albumin		Globulin		Blood Volume, Cc.			Hematocrit	Hemoglobin	Mean Blood Pressure, Mm. Hg
				Serum, per Cent	Entire, Gm.	Serum, per Cent	Entire, Gm.	Serum, per Cent	Entire, Gm.	Red Blood Cells	Plasma	Whole			
T 142	Control	0	...	5.56	44.8	3.13	25.3	2.43	19.5	(424)	(806)	(1,230)	34.5	81.6	118
16.4 Kg.	1 hr.	164	...	5.38	23.8	2.82	12.2	2.66	11.6	457	443	900	50.8	111.5	80
	2 hr. 30 min.	410	...	4.80	29.1	2.44	14.8	2.36	14.3	459	606	1,065	43.1	94.3	118
	4 hr.	656	1.6	4.39	30.2	2.28	14.3	2.11	15.9	452	688	1,140	39.6	88.2	118
	5 hr. 30 min.	...	...	4.93	32.4	2.04	13.4	2.89	19.0	460	657	1,117	41.2	89.8	110
	7 hr.	...	...	5.11	32.1	2.60	16.3	2.51	15.8	469	628	1,097	42.7	91.5	97
	Injected blood	...	...	6.01	....	3.48	....	2.53	....	...	...	.....	31.2	80.2	
T 145	Control	0	...	6.70	63.3	3.84	36.2	2.86	27.1	(881)	(944)	(1,825)	48.3	116.2	150
18.8 Kg.	1 hr.	188	...	6.32	55.9	3.48	30.8	2.84	25.1	895	885	1,780	50.3	119.0	120
	2 hr. 30 min.	470	...	6.52	55.4	3.54	30.1	2.98	25.3	915	850	1,765	51.9	120.0	136
	4 hr.	752	1.9	5.99	55.0	3.24	29.7	2.75	25.3	927	918	1,845	50.2	115.0	137
	5 hr. 30 min.	...	...	6.30	55.5	3.45	30.4	2.85	25.1	914	881	1,795	51.2	118.1	126
	7 hr.	...	...	6.32	51.3	3.45	28.0	2.87	23.3	928	812	1,740	53.3	122.0	117
	Injected blood	...	...	7.64	....	3.78	....	3.86	....	...	...	.....	37.0	85.3	

Protocols.—T 142: Morphine was used as anesthetic. A small amount of gum acacia solution was introduced intravenously in order to cause the decline in blood pressure. As soon as a decline in blood pressure was initiated, the introduction of salt solution containing epinephrine was commenced.

T 145: Morphine was used as anesthetic. Following the control determinations 7 cc. of 6 per cent gum acacia was introduced intravenously. The blood pressure declined to 75 mm. and remained there for a few minutes. As soon as the blood pressure began to decline, the introduction of salt solution containing epinephrine was commenced.

from 0.1 to 0.3 cc. per kilogram of body weight. The various determinations were performed one hour, two and one-half hours and four hours following the beginning of the introduction of fluids, and also one and one-half hours and three hours following the termination of the injections.

RESULTS

Twenty experiments were performed. The mean arterial blood pressure was maintained at a level of less than 100 mm. of mercury in all of the experiments in which histamine was injected. In approximately one half of the experiments in which the decline in pressure followed the introduction of acacia or of blood, there was a return shortly thereafter to the previous control level. In the remaining experiments the pressure remained definitely depressed. In all experiments there were a decrease in the volume of plasma, a diminution in the percentage of protein and a marked decrease in the absolute amount of plasma protein. The results do not differ from those of the experiments reported previously in which solution of pituitary and epinephrine were not injected. However, it was necessary to use larger amounts of histamine in the present experiments in order to keep the blood pressure at a low level. The results of the experiments in which solution of pituitary or epinephrine was introduced with the salt solution into animals in which the unexplained decline in blood pressure occurred are given in tables 1 and 2. The findings in the other experiments did not differ from these.

SUMMARY

Experiments were performed in which a decline in blood pressure was produced by the introduction of histamine, of unpurified acacia and of incompatible blood, and salt solution was injected continuously intravenously. The introduction of solution of pituitary or of epinephrine in the amounts used in these experiments did not prevent the loss of protein from the circulation.

FORTY-NINTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

JOHN G. KUHNS, M.D.

EDWIN F. CAVE, M.D.

SUMNER M. ROBERTS, M.D.
AND
JOSEPH S. BARR, M.D.
BOSTON

JOSEPH A. FREIBERG, M.D.
CINCINNATI

JOSEPH E. MILGRAM, M.D.
NEW YORK

GEORGE PERKINS
LONDON, ENGLAND
AND
PHILIP D. WILSON, M.D.
Advisory Editor
BOSTON

(Concluded from page 168)

MISCELLANEOUS CONDITIONS

Osteochondritis Dissecans Capituli Radii.—Nielsen [22] reported 3 cases of osteochondritis dissecans occurring in the radial head. In each case the defect occurred on the inner articular margin of the head of the radius. There was no history of trauma. Clinically, there were weakness, severe pain in the elbow on motion, blocking motion and muscular atrophy. Roentgenologically and at operation, the typical appearance of the loose body with a defect in the articular surface was observed. In the author's clinic, during the past seven years, operations were performed in these 3 cases of osteochondritis dissecans in the radial head and in 35 cases of osteochondritis dissecans in the humeral head.

Avulsion of the Anterior Superior Iliac Spine.—Rothbart [23] reported, with x-ray illustrations, 2 cases in which the anterior superior spine of the ilium was torn off by indirect violence and displaced. Only 1 other case, reported by Köhler, is recorded in the German literature.

22. Nielsen, A.: Acta chir. Scandinav. **69**:305, 1932.

23. Rothbart, L.: Zentralbl. f. Chir. **59**:781, 1932.

[ED. NOTE.—One of the editors has recently seen an example of this injury in a stout boy. The injury occurred during a foot race.]

Rupture of the Pectoralis Major.—Borchers and Tontscheff [24] reviewed the clinical findings in rupture of the pectoralis major muscle. This injury is most apt to occur when an external force strikes the muscle at a time when it is in a state of contraction. A visible flattening and loss of function are the outstanding signs of rupture in the muscles.

Mechanics of Muscular Contractures in the Wrist and Fingers.—In discussing muscular contractures of the wrists and fingers, Steindler [25] emphasized the biophysics of the condition and attacked the problem under four headings, as follows: (1) the paralytic contractures, including those due to infantile, obstetric and peripheral paralyses; (2) the innervational contractures represented by the spastic paralyses; (3) the histochemical or ischemic contractures, and (4) the arthrogenic contractures, or those subsequent to an arthritic process and resulting not from the inherent muscle contracture alone, but from gravity and external resistances. The mechanism of development of each type of contracture was carefully discussed. In the treatment of any such contracture, Steindler would exhaust every effort of conservative treatment, consisting of stretching and muscle training, before resorting to operative measures. The procedures for the operative release of contractures mentioned by the author were: (1) lengthening of the tendon, (2) stripping of the tendon, (3) the injection of alcohol and resection of the motor nerve, (4) juxta-articular osteotomies and (5) simple myotomies.

Rupture of the Long Extensor Tendon of the Thumb.—A case of rupture of the tendon of the long extensor of the thumb was reviewed by Lapeyre.[26] The patient, aged 55, suffered from pain and swelling following a fall on the extended wrist. Twelve days later there was a sudden sharp pain in the thumb, and from that time on the second phalanx of the thumb could not be extended. The normal contour of the extensor tendon was absent. The ruptured end of the tendon was not felt. X-ray pictures showed a fracture of the lower end of the radius without displacement. Operation was refused. The author stated that rupture of this tendon falls into two categories: (1) spontanous ruptures without a history of injury; all the cases reported in this group occurred among military drummers; (2) ruptures following trauma, usually a fracture of the lower end of the radius. Twenty-eight cases of spontaneous rupture were reported. The lesions always occurred on the left side

24. Borchers, E., and Tontscheff, P.: Zentralbl. f. Chir. **59**:770, 1932

25. Steindler, A.: J. Bone & Joint Surg. **14**:1, 1932.

26. Lapeyre, J. L.: Presse méd. **40**:456, 1932.

among drummers who had been in service a long time. There was usually a history of swelling on the dorsal surface of the thumb of some duration. Then suddenly there was a slight sharp pain, occasionally a palpable snap, and the drumstick fell out of the hand. Some ruptures were incomplete; others were complete. In all cases it appeared that the tendon had undergone some weakening change, such as a tenosynovitis. Fifty-one cases of traumatic rupture were reported. The majority of patients were elderly. Thirty-nine cases were accompanied by fracture of the lower end of the radius. This fracture was often insignificant. There was an interval of days and sometimes weeks between the injury and the rupture. The movement producing rupture was often slight. The essential symptoms were a slight snap accompanied by very little or no pain, followed by an inability to extend the distal phalanx of the thumb. The site of rupture was always close to the belly of the muscle. The mechanism of these ruptures was not definitely understood. The author believed that following trauma the tendon becomes strangulated in its sheath by rupture of the tenaculum tendinum containing the nutrient blood vessels. Without nourishment the tendon degenerated, became atrophic and ruptured during some slight movement of the thumb. Treatment was surgical, with repair of the ruptured tendon. Conservative methods were successful only in the few cases in which rupture was partial.

Rupture of the Extensor and Flexor Pollicis Longus Tendons Following Colles' Fracture.—Two cases, 1 of rupture of the extensor pollicis longus tendon and the other of rupture of the flexor pollicis longus tendon, were reported, and the literature concerning 27 cases of the former was reviewed by McMaster.[27] The author was unable to find any reported cases of rupture of the flexor pollicis longus tendon. Both of the author's cases followed Colles' fractures. One occurred approximately one month after the fracture, and the second four months after injury. Both came on spontaneously without pain and without direct injury. Disability in using the thumb was the outstanding symptom in both cases. There was no pain. In regard to the cause of this condition, the author suggested two possibilities: (1) partial severance of the tendon by a sharp edge of bone at the time of the fracture, or (2) local tendon necrosis due to a disturbed blood supply. Both patients recovered completely after an open operation.

OPERATIONS ON THE BONES, JOINTS AND TENDONS

Translocation of Tendons.—Von Baeyer [28] described what he called translocation in preference to transplantation of tendons because of the

27. McMaster, P. E.: J. Bone & Joint Surg. **14**:93, 1932.

28. von Baeyer, H.: Zentralbl. f. Chir. **58**:3140, 1932.

relatively simple technic of the former. The use of this procedure in four situations was discussed: (1) In paralysis of the calf muscles with good peronei, a groove was made in the long axis of the tendo achillis, in the tuberosity of the os calcis on the lateral aspect. The tendon of the peroneus longus was translocated or dislocated into this groove. The tension of the muscle produced an equinus deformity, which disappeared in a few weeks. It soon functioned normally in the new location. (2) In paralysis of the tibialis anterior with a good extensor longus hallucis, a groove was made on the scaphoid in its medial plane. The extensor longus hallucis tendon was translocated into this groove, and the foot was immobilized in supination with the great toe in a neutral position. (3) In palsy of the quadriceps muscle, the sartorius was attached to the atrophic patellar ligament, and one or the other of the internal hamstrings was also transplanted. (4) In habitual dislocation of the shoulder, the long tendon of the biceps was freed and the intertubercular sulcus of the humerus was deepened and lengthened to the center of the humeral head. The tendon of the long head of the biceps muscle was translocated into this groove.

[Ed. Note.—Procedures 1 and 2 are new to the editors. Procedure 3 is a tendon transplantation which is carried out in many clinics in this country and abroad. Procedure 4, while similar to the Nicola operation, has the disadvantage of injuring the articular cartilage.]

Plastic Repair of the Anterior Crucial Ligament.—Porzelt [29] devised a procedure for the repair of the anterior crucial ligament. A pedicled ligament was obtained from the inner aspect of the joint capsule, leaving it attached at its base. This ligament was brought through the tibia and sewed to the portion of the anterior crucial ligament still attached to the femur. The articular capsule was repaired. Good functional results were reported.

[Ed. Note.—It is questionable whether operations that attempt repair of the crucial ligament to correct instability of the knee joint should be advocated. In the cadaver, at least, the lateral ligaments seem to be of much more importance, since division of the anterior crucial ligament through a punctate incision in the capsule by one of the editors produced little instability. The recovery of stability in the joint after rupture of a crucial ligament seems to depend chiefly on the lateral ligaments of the knee joint and on muscle tone.]

Operation for Obstetric Paralysis.—Kleinberg [30] reported 8 cases of obstetric paralysis, of the upper arm type, in which he performed an operation consisting of subperiosteal reflection of the external rotators

29. Porzelt, W.: Zentralbl. f. Chir. **59**:658, 1932.

30. Kleinberg, S.: Reattachment of the Capsule and External Rotators of Shoulder for Obstetric Paralysis, J. A. M. A. **98**:294 (Jan. 23) 1932.

and a portion of the capsule of the shoulder joint for a distance of two-thirds the circumference of the humerus. The subscapularis was also resected subperiosteally. The arm was put in a position of abduction and external rotation. The structures then reattached themselves in their new positions. In the discussion which followed, Sever pointed out the importance of also dividing the pectoralis major tendon, and he said that frequently the coracobrachialis was a deforming factor.

Surgical Approach in Old Posterior Dislocation of the Elbow.—Van Gorder [31] described his technic for operative reduction of an old posterior dislocation of the elbow. It consisted essentially in dividing the triceps tendon transversely one-half inch (1.27 cm.) above the olecranon. The ulnar nerve was exposed and carefully protected. Adhesions were then freed and the dislocation gently reduced. The divided triceps tendon was then sutured either with fascia lata or with a portion of the Achilles tendon. Active exercises were started two weeks after operation. Five cases were presented, with illustrations.

Operative Procedures for Paralytic Talipes Calcaneus.—Whitman [32] was opposed to transplantation of the tibialis posticus and peronei muscles for the correction of paralytic talipes calcaneus as advocated by Lange.[33] He advised astragalectomy for this condition. He considered the astragalus the key of the deformity, and he thought that backward displacement of the foot and the contact between the tibia and fibula and the tarsal bones secured lateral stability and checked dorsal extension of the foot, thus supplying the resistance essential for normal gait. He referred to Miltner,[34] who, in 112 cases in which astragalectomy was performed, reported good results in 101 cases, fair results in 6 and poor results in 5.

FRACTURES

Marching Fractures of the Metatarsal Bones.—Straus [35] reported a case of unrecognized marching fracture, or spontaneous fracture of the second metatarsal bone, in an obese woman. X-ray pictures taken before operation showed no fracture, but new bone formation. An exploratory operation showed an old transverse fracture of the metatarsal bone surrounded by callus. The author reviewed various hypotheses concerning the etiology. He suggested that if the fatigued muscles failed to support the osseous structures of the foot, fracture might occur.

31. Van Gorder, G. W.: J. Bone & Joint Surg. **14**:127, 1932.
32. Whitman, R.: J. Bone & Joint Surg. **14**:242, 1932.
33. Lange, F.: J. Bone & Joint Surg. **13**:479, 1931
34. Miltner, L. J.: J. Bone & Joint Surg. **13**:502, 1931.
35. Straus, F. H.: Surg., Gynec. & Obst. **54**:581, 1932.

[Ed. Note.—This case is of interest, since amputation of the foot was suggested on the assumption that a malignant condition existed. These cases may simulate malignant periosteal lesions and may be so diagnosed because a history of trauma is absent.]

Treatment of Central Luxation of the Femur.—Babini [36] discussed the treatment in central dislocation of the femoral head. Two cases were reported in which the lesion followed a severe fall on the greater trochanter of the affected side. Reduction, with a satisfactory end-result, was obtained in both cases by skeletal traction on the greater trochanter with counter-traction on a plaster spica.

Fractures of the Knee, "Bumper Type."—Carey [37] described a method of closed reduction in fractures about the knee commonly called the "bumper type." The method consisted of manual reduction of the fibular head and replacement and reshaping of the tibial condyle with a mallet. Plaster immobilization was continued for three weeks, when physical therapy was begun. Weight bearing was permitted in from nine to eleven weeks. Forty-five cases were reviewed. The mechanics of the production and associated injuries were discussed. The author thought that a rupture of the external lateral ligament should be assumed to be present in many cases.

[Ed. Note.—In the editors' experience, the internal lateral ligament is the one usually injured.]

Treatment of Compression Fractures of the Articular Surface of the Tibia.—Hultén [38] stated that pain occurred about the knee if a condyle of the tibia was permanently displaced downward from 0.5 to 1 cm. after fractures. When attempts at closed reduction did not secure the normal anatomic relationship, open reduction was advocated. For old cases he described a method of driving in a bone wedge from the tibia into the lowered condyle to level the condyles.

Longitudinal Fractures of the Patella.—Lapidus [39] called attention to the not infrequent occurrence of longitudinal fracture of the patella, and pointed out that such an injury frequently went unrecognized because of failure to take proper x-ray pictures. The writer reviewed the literature and collected the cases of 13 patients treated by himself or his colleagues in two years. In 9 of these cases the fracture was in the usual place, i. e., in the junction of the outer and middle quarters of the patella. He thought that most such fractures were produced indirectly by muscular pull with the knee flexed, thus producing pressure between the femoral condyle and the outer pole of the patella. It was

36. Babini, R.: Chir. d. org. di movimento **16**:546, 1931.
37. Carey, N. A.: California & West. Med. **36**:226, 1932.
38. Hultén, O.: Zentralbl. f. Chir. **59**:344, 1932.
39. Lapidus, P. W.: J. Bone & Joint Surg. **14**:351, 1932.

important to differentiate such a fracture from a congenital anomaly. In order to demonstrate a longitudinal fracture of the patella, he suggested taking a roentgenogram by placing the anterior aspect of the thigh on the x-ray film and flexing the leg on the thigh.

Os Trigonum and Fractures of the Posterior Aspect of the Astragalus.—Ghigi and Morelli [40] dissected 80 cadavers, and in 35 feet a posterior astragalar process longer than 5 mm. was found. In 16 feet a smaller process was noted. In 2 cases a posterior process was covered with articular cartilage. In only one instance was an os trigonum found. The authors, therefore, found a well developed posterior astragalar process in 21.8 per cent of the ankles. Sixteen cases, 1 bilateral, of fractures of the posterior astragalar process were reported, 9 in detail. Several cases occurred in conjunction with adjacent fractures. The fractures caused acute pain in the ankle, swelling and tenderness. Complete recoveries followed immobilization. Shepher, in 1882, first described this fracture. A review of the literature was given.

Late Results in Fractures of the Olecranon.—Madlener and Wienert [41] reviewed 36 cases of fracture of the olecranon. In 24 of these cases an operative reduction was performed, and 12 patients were treated conservatively. Wire was used for suture in the operative reductions. Better functional results were observed in the patients treated conservatively. In the group requiring operation, the results were good in only slightly more than half of the cases. In 14 of 22 patients examined from two to nine years after treatment, an arthritis deformans had developed.

Colles' Fracture.—Carp [42] analyzed the roentgen findings in 100 cases of Colles' fracture accompanied by fracture of the ulnar styloid and correlated them with anatomic dissections in an effort to ascertain the cause of the fracture of the ulna. He concluded that fractures at the base of the ulnar styloid were due to the pull of the displaced intra-articular fibrocartilage of the wrist joint, and at the middle and tip of the styloid by the pull of the ulnar collateral ligament.

Slipping of the Upper Femoral Epiphyses.—Ferguson and Howorth [43] reported their observations in 70 cases of slipping of the upper femoral epiphysis observed at the New York Orthopedic Hospital. Sixty-three cases were seen in adolescent patients, while 7 were observed

40. Ghigi, G., and Morelli, A.: Chir. d. org. di movimento **16**:499, 1931.

41. Madlener, M. J., and Wienert, B.: Arch. f. klin. Chir. **168**:577, 1932.

42. Carp, L.: The Roentgenologic Displacements in Colles' Fracture: With Special Reference to the Mechanism of the Accompanying Fracture of the Ulnar Styloid; A Report of One Hundred Consecutive Cases, Arch. Surg. **24**:1 (Jan.) 1932.

43. Ferguson, A. B., and Howorth, M. B.: Slipping of the Upper Femoral Epiphysis: A Study of Seventy Cases, J. A. M. A. **97**:1867 (Dec. 19) 1931.

in "adult residuals." Fifteen cases were bilateral. The age of onset ranged from 8 to 15 years. Only 65 per cent of the patients were overweight. Trauma, as a rule, was trivial as an etiologic factor. The theory of infection was suggested as a possible cause. The early signs and symptoms in the "preslip stage" were enumerated, and the means of diagnosis both from the physical examination and from the x-ray plate were described. In regard to treatment, of 21 attempted closed reductions, 18 failed, 6 cases later coming to open operation. In 11 cases open reduction was attempted, with fair anatomic success in only 3. In five of the 11 cases the head was freed at the epiphyseal line, while in 6 cuneiform osteotomy was performed near the epiphyseal line. In 4 cases subtrochanterian osteotomy was done when there was a displacement of from five-eights to seven-eighths inch (0.9 to 1.5 cm.). The authors favored the open operation, with drilling of the femoral neck across the epiphyseal line in young patients in the preslip stage. They felt that no serious interference with growth would occur. They regarded the preslip stage as a real emergency, and favored absolute rest in bed or open operation with drilling.

Repair of Ununited Fractures of the Neck of the Femur.—Magnuson [44] advocated an operation which he believed restored the normal weight-bearing lines and anatomy more nearly than the various other operations designed to improve this common disabling condition. The ununited head of the femur was hollowed out with a burr so as to form a cup the deepest part of which was pointing upward rather than at the center of the hip joint. The trochanter was then removed, and the stump of the neck was remodeled so as to fit into the cup-shaped head. The trochanter was then reattached to the femoral shaft. Weight bearing was started in eight weeks.

Lateral Dislocation of the Vertebrae.—Lawson [45] reported 3 cases of lateral dislocation of a vertebra. The first and third patients were seen shortly after injury, while the second patient was observed four months after the original trauma. An attempt was made to reduce the dislocation by open operation in the first instance, but this was unsuccessful. The second patient was untreated, and no mention was made of the treatment in the third case. In all cases, accompanying the dislocation there was extensive damage to the laminae and the transverse processes. In the first case, the dislocation was of the fourth lumbar segment on the fifth sacral vertebra; the second case presented dislocation of the fifth lumbar segment on the first sacral vertebra.

Vertebral Fractures Without Injury to the Cord.—In a series of 215 patients with fractures involving the spinal column collected by

44. Magnuson, P. B.: The Repair of Ununited Fracture of the Neck of the Femur, J. A. M. A. **98**:1791 (May 21) 1932.

45. Lawson, J. D.: J. Bone & Joint Surg. **14**:387, 1932.

Conwell,[46] there were 100 patients with vertebral fractures without injury to the cord. From these 100 cases he drew the following conclusions: Immediate splinting of the injury is important; when a spinal fracture is suspected, the patient should be transported prone. Negative x-ray pictures immediately after injury do not always rule out fracture; in a number of cases, later vertebral collapse may be observed. Complete reduction of the fracture is desirable, but is not always necessary for a good functional result. Later collapse may occur after reduction.

Operative fusion is indicated, particularly if there is delayed healing of the fracture and severe persistent pain. Fusion, however, does not always relieve the pain. Osteo-arthritis is commonly observed as a complication in patients over 40. Manipulative reduction under general anesthesia is necessary in only a few cases. In most instances reported, gradual hyperextension of the spine was used, with an adjustable convex Bradford frame, for fractures with compression of the anterior portion of the vertebral bodies. When reduction was accomplished, a plaster case was molded to the body. Conwell advised immediate reduction of the fracture dislocation of the cervical vertebrae, followed by fixation in a plaster cast. When there is great danger of injury to the cord, he advised constant traction. Dislocation of the dorsal and lumbar vertebrae is best treated by constant traction.

Manipulative Reduction in Fractures of the Spine.—Davis[47] gave the subsequent course in several cases of spinal fracture followed up for five years in which his method of combined passive and active hyperextension of the spine was used. No late changes occurred in the reduced spinal fractures. Emphasis was placed on an immediate decision in fracture of spines with paralysis as to whether laminectomy or reduction should be done. The author thought that in the great majority of cases reduction of the impacted fracture of the centrum of the vertebra, thereby enlarging the neural canal, is of more importance than laminectomy, as it accomplishes a similar purpose without altering the deformity.

[ED. NOTE.—The value of Davis' manipulative reduction of spinal fractures is unquestioned. Since his original article many cases have been handled successfully by others. This method, without doubt, shortens convalescence and is accompanied by a higher percentage of complete recoveries.]

New Method of Treating Fractures Using the Well Leg for Counter-Traction.—Anderson[48] described a method of treating fractures of the pelvis, femur and tibia in which skeletal traction is made

46. Conwell, H. E.: South. M. J. **25**:141, 1932.

47. Davis, A. G.: Am. J. Surg. **15**:325, 1932.

48. Anderson, R.: Surg., Gynec. & Obst. **54**:207, 1932.

on the injured leg, the well leg being used for counter-traction. A plaster cast is applied on the well leg from the toes to the groin. To this a counter-traction stirrup is applied. On the injured side a pin is inserted through the tibia and attached to a stirrup. The injured leg is incased in a plaster cast which extends to the knee. The transverse lever that connects the traction and the counter-traction is then adjusted through a rod with a spring and turnscrew. A locknut at the end of the traction stirrup controls the rotation of the leg. The author claimed for this method ease in after-care, certainty of immobilization and greater comfort for the patient.

RESEARCH

Regeneration of the Hyaline Cartilage.—Santos [49] was able to demonstrate microscopically regeneration of hyaline cartilage in a series of femoral heads following complete intracapsular fracture. This occurred in the central area not covered by perichondrium as well as peripherally, and was often preceded by invasion and resorption of the dead cartilage by the subchondral bone marrow. The formation of new cartilage proceeded partially from the pannus covering the joint, but chiefly from proliferation of surviving hyaline cells, usually in the deeper layers of the cartilage.

49. Santos, J. V.: Surg., Gynec. & Obst. **54**:650, 1932.